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CASES OF MYXŒDEMA AND ACROMEGALIA TREATED WITH BENEFIT BY SHEEP'S THYROIDS:

RECENT OBSERVATIONS RESPECTING THE PATHOLOGY OF THE CACHEXIAS FOLLOWING DISEASE OF THE THYROID; CLINICAL RELATIONSHIPS OF GRAVES'S DISEASE AND ACROMEGALIA.

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Case I. is that of an unmarried lady, now forty-eight years old, and always of delicate health.

I was first called to see her in December, 1885, and at the time of my visit the diagnosis was beyond question, even from her appearance alone.

She had taken cold while menstruating during a visit to the Philadelphia Exhibition of 1876, and it is possible that this was the starting-point of her sickness, though she was then pronounced only severely anæmic, and the myxœdemic symptoms were not noticed until 1880 or 1881. The family history on the mother's side was markedly neurotic.

The face was clayey-gray, with a yellowish tint, the skin thick, stiff, dry, and coarse. The lips were protuberant and thick, and moved each in one piece, as it were, as she talked. The eyelids were swelled and alabaster-like in appearance, especially the upper, which overhung the eyes so that at times she had to throw the head back a little in order to see. The neck was thick, the hands were large, scaly, and dry, and a similar dry and coarse condition of the skin was everywhere present.

The nutrition of the teeth and nails was defective, and the hair had fallen out except for a few bunches here and there.

Formerly slender and with delicate coloring, she now looked overgrown and old. The limbs were large but not strong, and the skin was so inelastic and so tightly stretched over the legs below the knee, that the masseuse found it impossible to use the ordinary methods of manipulation. No true œdema was noted at this time, but at a later period the ankles pitted deeply on pressure. The swelling of the eyelids was partly watery, and increased during the night toward the side on which she lay.

The pulse was but 60; the heart-sounds free from murmur, but exceedingly feeble. There was a tendency of the head to droop forward, so that it was

with an effort that she held it erect. The voice was husky and the tongue thick. The gait was slow and insecure, so that she often stumbled and sometimes fell. She felt weak, and became breathless on slight exertion.

The mental condition was no less striking than the physical. An inconquerable inertia and apathy imprisoned her thought, feeling, and action, so that she could neither plan nor execute effectively, and every trifling duty seemed a mountain to climb; and yet her ineffectiveness did not fill her with real despondency.

Her friends would leave her with one boot on and the other in her hand, and return an hour later to find her in the same condition and attitude. Or what she held would slip from her grasp and she would not stoop to pick it up. Or, at times, she would lean in a stupor against the mantel-shelf, and remain motionless for one or two hours. The nearest duties often passed unfulfilled, and the thought of them failed to rouse her. Yet in spite of her slowness, and lethargy, and lack of initiative, she was neither melancholic nor demented, and would converse intelligently and pleasantly, though without animation, on many subjects. It is interesting to note (see below) that a certain degree of this apathy and slowness was characterstic of her temperament even many years before her illness began.

She slept all night, though often troubled with distressing dreams, but was constantly drowsy in the day. She suffered much from constipation, and later from hemorrhoids, and had an offensive expectoration, which no doubt contributed to give the breath the cadaveric odor which then characterized it.

The menstruation was at that time regular, but profuse; later it became very irregular, and was absent for months together, and her periods would leave her much weakened.

The urine was habitually very pale, and of low sp. gr., free from albumin and sugar. All the solid constituents were diminished, the amount of urea being 11.78 grm. to the litre (Prof. E. S. Wood).

The thyroid could not be felt. The skin was cool to the touch; and the temperature usually ranged around 95° F. Several times it almost touched 94°; and 97° was rarely, if ever, passed, even in slight sickness.

Blood-counts made during March and April, 1886, showed 3,120,000; 3,200,000; 3,234,000; 4,240,000. The proportion of whites was normal.

The next four years brought little change, except that in winter she would be worse, in summer better.

In the summer of 1891, however, a new symptom showed itself, namely, a synovitis with great external swelling, first of one knee, then of the other, brought on by a trifling shock or wrench, due to stepping heavily, the first time out of a carriage, the next time out of a horse-car. In one of the cases reported very early by Dr. Ord, the rupture of both patella tendons occurred in a similar manner, and the excessive swelling has been several times observed. The synovitis ran a very indolent course, and the appearance of the knee, with its thickened tissues, was so peculiar as to suggest the presence of some other process than simple effusion.

Up to the 1st of June, 1892, no treatment had brought material benefit, though persistent massage had given the patient much comfort. In June, 1892, I began a series of tri-weekly injections of a glycerin and carbolic extract of the sheep's thyroid, prepared as recommended by Dr. Murray.

Slight signs of improvement began to show themselves by the end of one or two weeks. In the course of six weeks the improvement in color, strength, and manner attracted the attention of everyone who knew her, even the children of her neighborhood, and was further confirmed by the appearance of a growth of fine hair all over the head, and a marked rise in pulse and temperature.

The temperature varied, but by the end of August, perhaps earlier, it ranged pretty constantly between 96° and 97° F. Menstruation, which had been absent so long, recurred in July, August, and September, but such recurrences had occasionally showed themselves, and it was still profuse and painful.

The swelling of the eyelids varied in amount, but during August it was almost absent, and that of the ankles had greatly lessened.

With the advent of the colder weather of September and October, I saw with regret that her improvement, hitherto steady, seemed to have suffered a check. She began to look pale and to feel languid, the swelling of the eyelids reappeared, and she complained of pain in the chest on slight exertion. Attributing this in part to an interruption of the treatment during the first ten days of October, I tried giving the injections more frequently than ever, part of the time almost daily, though at first without marked effect.

In November she began the treatment by the mouth, as recommended by Mackenzie and by Howitz, of Copenhagen, and took five or six sheep's thyroids a week (or more strictly, five or six lobes, as the sheep's thyroid consists of two separate lobes).

During the next month, and even after the final stage of improvement had been fairly entered upon, she complained much of a sense of thumping in her head, and while her mental condition was becoming steadily more natural, her appetite and strength seemed for a time rather to fail.

Ever since the outset of the treatment, she had noticed at times a sense of flushing and dizziness after the injections, such as has been noted in the reports of some of the English cases, but neither this effect nor the increased secretion of urine which others have noted was at all striking.

On December 9th, an estimation of the hæmoglobin by Fleisch's apparatus gave 55 per cent. Toward the end of December there was another period of depression in which she complained of increased thumping in the head and ears, and of nausea and languor, especially in the morning. These symptoms seemed at least partially attributable to an excess of thyroids, of which she had taken four glands a week, though these periods of depression did not invariably attend the use of the larger amounts.

This sense of illness was, however, attended by a rise of pulse and temperature rather than a fall, the pulse reaching 78 on December 18th, and the temperature 98°. And furthermore, it was plain that the whole character of her nutrition was becoming more normal, though it was not in all respects satisfactory. On December 21st, when I had not seen her for nearly three weeks, it was evident at the first glance that the condition of myxœdema was giving place to one of simple anæmia. She complained a great deal at this time of itching, which others have noticed likewise, perhaps from the action of the thyroids, but more probably from the changes taking place in the skin.

It was difficult to say whether she had actually grown paler or less pale, so unlike was her present complexion to that of the clay-like mask that she had worn so long. Unfortunately, she could not easily be weighed, but it was clear that she was rapidly growing thinner and slenderer, while her hands were becoming softer and more shapely. The clothes that she had worn were now hanging in folds, and in fact she became at this time really too thin, and with still further improvement she has gained flesh somewhat.

The opening of the new year was marked by her discarding her wig in favor of her new growth of dense and soft hair (now about four inches long) and by her beginning to take the thyroids in the form of powder, skilfully prepared by Parke, Davis, & Co., at my suggestion.

I had been in correspondence with them for this purpose for a number of weeks, and did not learn until later that similar methods were being adopted in Sweden and England. Fifteen grains of this powder represents one lobe of a sheep's thyroid. The taste is found nauseous by some patients, and does not disappear for many hours. These objections are mainly obviated by the use of capsules, or of keratin-coated pills, which do not dissolve in the stomach.

Not only had her face and figure by this time changed so that acquaintances occasionally failed to recognize her, but her voice had grown markedly firmer and clearer, and her manner alert and responsive.

An accurate examination of the blood made by Dr. J. J. Thomas gave the following result:

Reds . .	5,700,000	Polynuclear whites	66.4 per cent.
White . .	7,000	Mononuclear " .	21.6 "
		Lymphocytes . .	10.04 "
Hæmoglobin	61 per cent.	Eosinophiles . .	2.0 "

No increase in size of reds. A few myelocytes.

The menstruation recurred normally and almost painlessly in January, February, and March and April, appearing exactly at the expected date. For two weeks in February and March she took no thyroids, and toward the close of that time there were signs of a recurrence of symptoms, a firm non-œdematous swelling appearing in the legs above the ankles. The mental condition remained good, and on resumption of the thyroid powders the slight swelling soon disappeared.

Since the treatment was begun, the neck, waist, and arms have diminished about three inches in girth, and the old shoes and gloves have, so to speak, discarded themselves. She is still an anæmic and delicate person, as she always was, but as regards any distinct myxœdema she is practically well.[1]

The temperature is usually normal, but occasionally runs half a degree too low.

CASE II. is that of a lady fifty-five years old, and is particularly interesting, both because the improvement was very rapid, and from the fact that previous to the onset of the myxœdematous symptoms, the thyroid was much enlarged, and moderate but constant tachycardia was present. The patient has been under the care of another physician, and I have seen her only incidentally except during the first period of the disease, when I tried for some time to reduce the size of the goitre by electrolysis. The case is also of interest from the fact that the patient's cousin and aunt had myxœdema in a pronounced form, and eventually died with it, the latter as an elderly person, the former in middle life. The aunt had been for many years crippled with rheumatoid arthritis.

The case seems to be one of those where an exciting cause of the disease may well have been anxiety and emotion, acting on an intense and sensitive temperament. The thyroid first began to enlarge about ten years ago. The tumor was unusually hard, much harder than the normal gland, and there were no vascular murmurs such as are often seen in Graves's disease. There was no exophthalmus, but the pulse was always moderately rapid—from ninety to one hundred and twenty. In view of the important question as to the possible relationship between Graves's disease and myxœdema, it is interesting to bear in mind that we have here a case where in the presence of a manifestly hereditary tendency to myxœdema, the first actual change was this thyroid disease, with at least one of the Graves's disease symptoms. (Perhaps, however, the tachycardia was purely reflex. See below.)

It is also a noteworthy fact that the patient's health failed considerably during the first period, and that besides dyspnœa, which may have been due to pressure, she suffered much from anæmia and debility. As her health had previously been good it is reasonable to suspect the thyroid disease as having been responsible for the falling off at this period, the more so that with the recent thyroid treatment not only the myxœdema but also the anæmia has for the most part disappeared. The myxœdematous changes first showed themselves two years ago, at the time of the menopause, and have been unmistakably characteristic; the presence of the alabaster-like swelling and pallor of the eyelids, lips, and face, the dryness of the skin, the increased size of the hands, the gross enlargement of the body, slightly subnormal temperature, thickness of the tongue, and slow speech leaving no doubt as to the diagnosis. The urine contained a trace of albumin, and occasionally a few casts. Mental changes have not been present.

[1] An examination of the blood made since this paper was written has shown that the anæmia has not improved of late, but rather grown severe, though in other respects the patient is doing well.

The treatment with the thyroid powder was begun about February 15th, since which time the patient has taken one powder of fifteen grains, which is the equivalent of one lobe of a sheep's thyroid, every second day.

The improvement was more rapid than in the first case, perhaps because the disease was less advanced and because the patient's previous health had been better. There is still some swelling of the legs, with ordinary œdema, but the patient's face has regained its delicacy and size and color of fifteen or twenty years ago. The thyroid is still large, though not so large as before. It will be very interesting to follow the condition of the urine in order to see whether the renal changes disappear. At present casts are still to be found, though they were absent in the three or four examinations made during the year previous to the beginning of the treatment.

I have also notes of three other patients who are taking the thyroids with benefit. One of them has acromegalia of rapid onset and typical form. No enlargement of the jaw is present, but the big hands and feet, rapid pulse, with tendency to palpitation and moderate muscular atrophy, place the diagnosis beyond question.

She came first to the out-patient department of the Massachusetts General Hospital, and was seen by Dr. G. M. Garland, who kindly gave me the opportunity of examining her. Later, she entered the wards, in the service of Dr. F. C. Shattuck, and there she improved somewhat under tonic treatment and sodium salicylate.

Some weeks after her discharge, however, I looked her up and found her still feeble and unable to work. Under fifteen grains of the thyroid powder every second day she has gained steadily, so that now, at the end of three weeks, she works with her hands for two hours daily.

Of the other two cases, one stands nearer to acromegalia, the other to myxœdema, though in both the diagnosis is doubtful. The latter is of especial interest from presenting atrophy of the optic nerves, which is more common in acromegalia than in myxœdema, though seen in the latter disease (Hun and Prudden, Wadsworth, Jones). The former is under the care of Dr. G. C. Stearns, of Leicester, but is taking thyroids at my suggestion. A letter received yesterday reports that the improvement goes steadily forward, both as regards general strength and the appearance of the face and lips.

There is a large swelling of the neck, probably a thyroid, which is diminishing in size under treatment; and, in fact, both patients consider themselves as decidedly better.

There are many questions of detail with regard to the new treatment by thyroid preparations which are of great practical importance. The following seem to me especially so:

Is the method by the stomach equally effective with that by injection, and is there anything to choose between the powder prepared

by evaporation, the gland itself, and the extract precipitated with alcohol as recommended by Vermehren?

Must the dose by the stomach be larger than that by injection, and, if so, for what reasons?

What is the cause and significance of the rapid loss of weight so often noted, and may it occur in ordinary obesity, or with healthy persons, under the use of thyroids?

What is the cause and significance of the other symptoms observed during the thyroid treatment, especially those of cardiac origin?

Are signs of renal irritation brought on or increased, and under what conditions?

Some of these questions can already be answered fairly well. The method by the stomach has not failed in any genuine case, and although one of the best of English observers at one time asserted that four or five times as large a quantity must be given to get the same effect as by subcutaneous injection, yet moderate quantities are sometimes so effective that we have no reason to conclude that any considerable part of the dose passes unabsorbed in most conditions of the stomach and intestine. Some good chemical or physiological test is, however, much needed to enable us to study these points and to compare the different preparations.

The loss of weight is an early sign of improvement, but it sometimes goes beyond the requirements of health; and this fact, coupled with the observations of Dr. A. Barron, of Liverpool, on the effects obtained in obesity,[1] suggests that the thyroid secretion may, under certain conditions, modify the tissue-changes even of healthy persons. A myxœdematous patient of Laache's lost more than nine kilogrammes, or about nineteen pounds, in three weeks, and my first patient must, at one time, have lost weight almost as rapidly.

Immediately after the injections, and even the stomach doses, of thyroid, there is sometimes a rise of temperature and pulse, increased secretion of urine, faintness or headache, and other symptoms; as the treatment goes on these symptoms may continue for a time, and may be associated with prostration, cardiac weakness; anginoid, neuralgic, or other pains (Laache), and even albuminuria (Laache). (Note also the increase in signs of renal irritation in my second case.)

[1] Dr. Barron has very kindly written to me that he has used the treatment in five cases of ordinary corpulence. One lost twenty-eight pounds in six weeks, three a moderate amount, and all lost more or less. I am trying it in two typical cases, but have no results to report as yet.

It is striking and important that these unpleasant signs sometimes last for weeks after the suspension of the treatment.

Dr. F. C. Shattuck will no doubt call attention to an important case which he kindly asked me to see with him, where attacks of palpitation with anginoid pain continued for several weeks after the cessation of a rather active, though short, course of treatment which had in other respects been remarkably effective for good. The fact that these effects last so long after the treatment by thyroids has been stopped, and that, on the other hand, they have failed to appear in some cases where large doses have been given, or at any rate do not necessarily appear at once (Vermehren) (my first patient has taken repeatedly thirty grains of the powder without noticeable effect), render it unlikely that they are wholly due to a direct action of the thyroid extract regarded as a drug. At any rate, other explanations suggest themselves as more probable.

One is that through an increased excitability of the cardiac centres, or from some other cause, the heart is called upon for increased action at a time when its muscular walls are in an abnormal state, or when its coronary arteries, which are liable to be thickened, are not supplying it with sufficient blood; another, that the products which are absorbed so rapidly from the diseased tissues act as irritants. It will be remembered that two of Murray's cases died while their improvement was in full progress, from sudden heart failure brought on by trifling exertion. One of these patients was known to have had cardiac disease, the other was assumed to have had a fatty heart.

At any rate, the action of the thyroid extract is not in all respects the same in health as in cases of myxœdema. Fenwick finds that diuresis does not occur in health, nor usually with myxœdematous patients unless they are under some slight excitement.

As regards the question of renal irritation, I would call attention to my second case, where, in spite of rapid improvement in other respects, the number of casts in the urine increased, and to Laache's case in which temporary albuminuria came on.

In another case, recently reported (Holman) the urine during treatment contained very large quantities of mucus.

Before leaving this part of the subject it must be noted that not only have the cases of myxœdema, successfully treated by animal thyroids, been gathering like a rising tide, but that myxœdematous cretins have likewise been shown to be susceptible of a considerable degree of improvement (Bramwell, Affleck, Carnwick, Gibson).

The point has not attracted as much attention as it deserves, that the "directly" hæmatopoietic functions of the thyroid, if they are of real importance, ought not to be met by ingestion of the thyroid secretion.

As a matter of fact, the anæmia of my first case does not seem inclined to pass away with the myxœdematous symptoms.

I shall confine myself, in what follows, to the pathological side of the subject.

To indicate, for reference sake, the percentage of frequency with which the different organs are diseased, I have arranged the results of the post-mortem examinations, including those published since 1888, in the form of a diagram, which, of course, must be taken as having only a relative and provisional value, since the autopsies are few, and the observations often incomplete and probably inaccurate.

I am not tempted to refer in detail to the varied anatomical changes to which the different organs are liable, because so little that is of fundamental importance has appeared since the able paper of Hun and Prudden and the report of the Committee of the Clinical Society of London in 1888, and especially since the masterly review of the functions of the thyroid by Horsley in 1890. Two experimental researches are, however, worthy of special mention. One is that of Hofmeister, who removed in young rabbits the main part of the thyroid, but not the glandules of Gley. This is supposed to leave the rabbits practically uninjured, and, indeed, their health does not apparently suffer, though the hair is apt to become a little coarse and the body relatively short and thick.

In fact, however, a series of other changes occur. The growth of the bones is checked; the epithelium of the convoluted tubules of the kidney is altered; the ovaries undergo a premature ripening, with an immense development of follicles. The hypophysis cerebri enlarges, but the spleen and thymus do not, and no histological changes were found in the central nervous system or in any of the abdominal organs.

The second research is by Capobianco, of the University of Naples, and has reference to the condition of the nervous system in the acute stage of the cachexia after thyroidectomy in dogs. They are fully confirmatory of the older observations of Rogowitsch, and show clearly how profoundly the circulation and nutrition of the brain, the medulla, the cord, and the nerve roots may be altered. The fact that other observers have found only circulatory changes, with œdema

(see Horsley's paper) or swelling of axis cylinders (Kopp), shows that there are great differences in the degree to which these results are produced, but for this very reason we should scrutinize carefully before giving the verdict, "normal"; and the more so when we recall that changes in the electrical irritability of the cortex cerebri (Schiff, Horsley) and the peripheral nerves (Awtokratow, Schwartz) are found.

The discovery by Hodge, of Clarke University, that simple fatigue leaves its mark on healthy nerve-cells—even physiological fatigue, as that of bees after their day's flight—should be borne in mind in this connection. Not only do these observations show the possibility of recognizing slight changes in nucleus and protoplasm, but they point out—what is too little regarded—that in estimating the effects of poisons or of other causes of impaired nutrition upon the central nervous system, we ought to know what conditions as regards exertion and fatigue had been present shortly before death. A man or animal who has taxed his poor or poisoned nervous centres will certainly have induced histological changes that otherwise would be wholly absent, and the exertion necessary for this result may be an amount which would ordinarily appear trifling.

It would be extremely interesting to see Hodge's experiments repeated on animals with the cachexia thyreopriva. The probability that positive evidences of an increased liability to fatigue would be found is foreshadowed by the experiments of Manfredi Albanese, which point to an increased susceptibility to fatigue on the part of the spinal cord in the serious condition which follows removal of the supra-renal capsules.

No doubt the case is different for the *chronic stages* of myxœdema and cretinism.

We do not know about liability to fatigue, but no histological changes were found, at any rate, by Hofmeister in his rabbits, or by such careful observers as Hun and Prudden in their cases of myxœdema. There are no histological changes, indeed, that are distinctly characteristic of the nervous centres of cretinism (Bourneville), though the arrangement of the convolutions is often peculiar.

Langhans and Kopp have made a careful study of the peripheral nerves after thyroidectomy and in cretinism, and have found a series of interesting and peculiar alterations in the endothelial cells of the perineurium and endoneurium, as well as in the lymph spaces and the bloodvessels, arranged in minute foci here and there, especially in the

nerves. The paper is one for histologists to discuss. Langhans at first thought these appearances to be peculiar to goitrous diseases, but this is very doubtful (Schultze, and Langhans himself).

The blood presents no constant changes except those of acute anæmia, and in the acute stages increased venosity (*v.* Horsley). The red cells have been found larger and also smaller than normal; the proportion of whites increased and normal; eosinophiles increased in one case (Ehrlich); myelocytes present in one (Case I.).

As to the final cause and nature of the changes which constitute myxœdema and cretinism, that is a riddle the solution of which we can approach but cannot reach. That the blood becomes toxic is inherently probable, and is confirmed by the fact that although usually harmless[1] if transfused into healthy animals, it precipitates the cachexia in the case of animals deprived of their thyroids (Fano, Zander, Rogowitsch, Fuhr); while, on the other hand, the cachexia may be mitigated by the infusion of healthy blood. Gley asserts that the toxicity of the urine is also increased.

The skin, the kidneys, the ovaries (Hofmeister, Langhans), the liver, the heart and pericardium, and other organs and tissues, also show signs of irritation and sometimes of degeneration. This is doubtless sometimes mucinoid in character, but mucin has not always been found, even in the skin, and Jürgens shows how complex the change which we call mucinoid really is. We do not yet know whether mucin, when it does occur, is merely a sign of degeneration or whether it is itself a poison. That it is the chief or only poison in myxœdema is highly improbable.

There are, moreover, some phenomena which seem to be less easily explained as the result of irritation and degeneration than as evidences of a sort of variation in structure, analogous, perhaps, to that which follows castration.

The curious fatty tumors of the neck so characteristic of myxœdema and myxœdematous cretinism are not easily accounted for as results of irritation; the changes in the ovaries of Hofmeister's rabbits were interpreted by him as a sign of follicular hypertrophy or premature ripening; the myxœdematous cretin is not only a diseased and degenerate individual, but may be regarded as a different variety, and this appears even in his mental characteristics.

If one looks for other instances of alteration of type with which to compare this, the most striking and, possibly, the nearest is that

[1] Gley finds the blood of dogs after thyroidectomy to cause convulsions in rabbits.

of eunuchism from castration, by which the bull is changed to the ox, and the cock to the capon. The analogy would be more significant if it could be shown by experiment that the effects of castration could be prevented by frequent injections of testiculin; indeed, the analogy would not hold if the results of this experiment turned out negative. So far as I know, it has never been tried, but it seems to me a reasonable experiment, and a logical outcome of the suggestive observations of Brown-Séquard and D'Arsonval.

The next point to which I wish to call your attention is with regard to the incomplete or partial forms of the thyroid cachexias.

The attention of physiologists and pathologists has hitherto been mainly directed to the study of the diseases due to complete, or nearly complete, destruction of the thyroid; and the opinion is current that the functions of the gland may be as well performed by a part as by the whole, because it has been found that when a piece of any considerable size is left, the cachexia does not, as a rule, occur. Usually the remaining piece grows larger. Sometimes the accessory glandules, which are ordinarily embryonic in character, also increase in size, and probably in efficiency, though they never grow to the size of the original gland. A compensatory enlargement of the hypophysis cerebri may also, it is thought, occur.

An additional argument that a part of a thyroid will serve for the whole is apparently furnished by the recent experiments of Beresowski. He removed enough of the gland to cause cachexia, and found that in the course of a few days distinct processes of repair had set in, as indicated by karyokinetic division of the glandular epithelium. This hyperplasia ceased, however, long before the piece of the thyroid had reached the full size of the gland, and the reason for this was supposed to be that the vital needs of the gland had been met.

In spite of the large amount of truth in these generalizations, it is in order to inquire whether we really have sufficient grounds for believing that the thyroid is so unnecessarily large, and, if this is not the case, whether we may not learn to discover and relieve diseased conditions associated with a partial destruction of the gland.

It is important to note, as indicating the complex nature of the problem, that myxœdema may fail to occur even when the true glandular epithelium of the thyroid has been replaced by a cubical variety, apparently secreting no colloid; and, indeed, a small part of a gland so altered may suffice. This is illustrated by the history of a case of Graves's disease reported further on in this paper, and by the experiments of Halsted and Welch upon dogs.

As regards the argument drawn from the cessation of the compensatory hypertrophy at a certain point, it seems to me extremely improbable that the amount of regeneration is exactly proportional to functional requirements. The law of repair is more complicated than this, and that is indicated in the present case by the fact that Ribbert found a true regeneration to follow the removal of comparatively minute pieces of the thyroid (see also Neumeister).

It would be an interesting research to see how much, or rather how little, of the thyroid must be removed before changes in growth and nutrition can be detected, especially in the light of Hofmeister's experiments, which show that rabbits may present them in spite of retaining, by the aid of their carotid glandules, apparently good health.

The studies of dosage during the treatment of cretinic children by sheep's thyroids, will no doubt throw much light upon this matter of the amount of thyroid secretion needed for full compensation, and meantime some clinical evidence is already forthcoming to show that the amount of thyroid sufficient for life, and fair health, is not necessarily sufficient for all the functions of the gland.

Some of the most important forms of cachexia from thyroid disease, not severe enough to cause myxœdema, are the following:

1. The early history of myxœdematous patients sometimes gives evidence of the presence of analogous forms of degeneration.

Two cases have been reported within a few years (Loewy, Merklen), where myxœdema came on when the patients were between twenty and thirty years old; yet both were of dwarf-like stature, and presented certain slight mental peculiarities which, without stamping them as cretins, suggested a congenital deficiency of thyroid action.

Struck by these cases, I turned to the abstracts published by the Committee of the Clinical Society to look up the early history of the patients who became myxœdematous before their twentieth year; that is, cases of myxœdema belonging to the period antecedent to senile involution, and I found these histories, incomplete though they are, to be of much interest. Four such cases are recorded, and in at least three of them, in spite of the scanty record of antecedents, there had been signs of degeneration, such as very low bodily weight; slight mental weakness; small, broad, and depressed nose; and extremely large tongue, indicating, perhaps, as in the cases first cited, a partial and unrecognized cretinoid state existing since childhood.

It is noteworthy that my first patient was not only anæmic and lacking in robustness, during her early life, but also showed some degree of the lethargic temperament which afterward became so very marked.

2. Cretinism is a disease of many degrees, and some of the cretins show a fair intelligence, a few a first-rate degree (comp. Bircher, and a celebrated case cited by Langhans). Yet their skulls are of the type now considered as probably, or possibly, characteristic of thyroid disease. In myxœdematous cretinism, which is the lowest type, characterized by unossified fontanelles and synchondroses (occasionally premature ossification), dwarf-like stature, tendency to umbilical hernia, etc., the thyroid is greatly atrophied, sometimes absent. In other forms the atrophy is only partial (Hanau), and portions of the gland may look healthy. Furthermore, the removal of a cretinic thyroid may cause myxœdema (Bircher).

3. Goitrous persons, in districts where the disease is endemic, are generally of inferior type, though, of course, it is not certain that the thyroid disease is the cause of this.

In my second case, which is probably typical of others, it is worth considering whether the anæmia and debility of the pre-myxœdematous, but goitrous, period may not have been an early stage of thyroid cachexia.

At any rate, myxœdema sometimes comes on quickly, but oftener slowly, and in the future it will be of great importance to learn to recognize the preliminary symptoms.

Another fact, of which we should never lose sight, is that myxœdema, or tetany, and perhaps other signs of the thyroid cachexia, may follow temporary disease of the thyroid, from which the patient eventually recovers, and may then pass away. Not only does this happen after partial thyroidectomy, but in the course of syphilis (Kocher), and as a result of ordinary goitre (*v.* Horsley's paper, 1890, *Brit. Med. Journ.*, 1890.)

As regards the question of the compensatory hypertrophy of the hypophysis, it is certainly true (Rogowitsch, Stieda, Hofmeister) that thyroidectomy done on dogs and rabbits is usually followed by enlargement of the hypophysis, which comes so near the thyroid in structure and origin, and it would seem also that the thyroid may enlarge after removal of the hypophysis (Vassale and Sacchi). On the other hand, it is not accepted as certain that this enlargement means increase of functional activity.

To express a complicated matter in a few words, it is generally conceded that the hypophysis contains two kinds of cellular bodies, the "chromophiles," and the Hauptzellen (Stieda and Rogowitsch), or "nucleated protoplasm" (Schönemann).

When the gland enlarges there may be found an increase in the number of chromophile cells, or an enlargement of the Hauptzellen; and there is almost always an increase in the colloid contents of the gland. The increase of the chromophile cells has been thought (Lothringer, *Arch. für mikroscop. Anat.;* cited by Vassale and Sacchi) to be of functional significance; but Schönemann, on the basis of a careful study of the hypophysis of a cretin, came to the opposite conclusion, namely, that the chromophile cells are degenerated forms, and are finally to be converted into colloid.

Vassale and Sacchi have recently made an ingenious experiment which seems to favor the view of Schönemann. Removing the hypophysis from an ox, they divided it into two parts; and while one of these was preserved in alcohol for comparison, to indicate the normal histology, the other was introduced into the abdomen of a rabbit and left for three days, presumably to undergo slow degeneration. The chromophile cells in the latter half were found to have increased greatly in number.

The same observers deny that the mere increase in colloid matter ought to be taken as a sign of increased functional efficiency, either in the case of the hypophysis or the thyroid, unless it is accompanied with indications of active cell-growth of the glandular epithelium, with karyokinetic appearances, and this, they declare, does not occur in either organ simply from extirpation of the other. They do, however, regard the two organs as physiologically similar, and this is important for the pathology of acromegalia, which seems to me a disease kindred to myxœdema, though the bond may be but that of a Scottish cousinship.

Hofmeister's experiments, which are especially valuable because his rabbits remained alive and well, and the hypophysis was given from three to six months in which to show its supposed compensatory growth, are confirmatory, as he thinks, of the observations of Rogowitsch and Stieda. He finds, as they did, not only an enlargement of the whole organ, but an increase in the size of the Hauptzellen.[1]

[1] There are several reasons for concluding that the colloid is not the important part of the thyroid secretion, but an envelope, or a by-product. Even its presence is not essential.

The valuable researches of Halstead and Welch, made some years ago, but not yet

The question is therefore still open for further research, but hereafter increased size cannot be taken as a sure sign of increased efficiency.

One suggestion thrown out by Hofmeister is worthy of comment, namely, that the large size of the sella Turcica, several times noted in cases of cretinism, indicates that the hypophysis had been hypertrophied. Klebs makes the same remark with reference to a case of acromegalia. As bony changes are, however, of regular occurrence in both of these diseases, the increased size of the sella Turcica admits of a different interpretation, and Schönemann distinctly notes that while the sella Turcica of his cretin was large, the hypophysis was rather small. Possibly it had been enlarged at an earlier period. Certainly the hypophysis is not always enlarged either in cretinism or myxœdema *at the period at which the post-mortems have been made.*

It is next in place to consider what other symptom-complexes, besides myxœdema, are associated with disease of the thyroid, and in what that association probably consists.

The diseases to be considered are exophthalmic goitre, acromegalia and certain forms of obesity.

1. The reasons for ranking Graves's disease among the thyroid cachexias were clearly set forth and ably championed by Moebius in 1891, and since then various writers have taken sides in the discussion (*v.* the abstracts by Moebius himself in Schmidt's *Jahrb.* for the past two years). Especially valuable are the monographs of Wölfler, of Gratz, and the able paper of Wette, who has had a large experience with thyroid diseases in all their aspects, as assistant in the surgical clinic at Jena.

It must certainly strike anyone who studies the matter, that there is a certain likeness between the acute nervous symptoms of the first stage of the cachexia following either complete or partial thyroidectomy, and the nervous symptoms of Graves's disease; and, on the other hand, a certain contrast between the latter and some of the symptoms of chronic myxœdema. This argument from the comparison of symptoms does not, however, fully stand close criticism.

published, show that in the regeneration of the thyroid which follows mutilation, the histological character of the gland may undergo great change. The epithelium tends to become high and cubical, instead of flat, and the colloid to disappear. Eventually the whole gland may be made to show this change. (See Trans. of the Assoc. of Amer. Physicians, 1893. Discussion on Myxœdema.)

A closely similar change has been noted by Councilman in a case of Graves's disease described farther on, yet this patient was not myxœdematous.

There is no real contrast, for example, between the sweating of Graves's disease and the dry skin of myxœdema, if the former is due, as is probable, to central excitation of the sweat nerves, and the latter to disease of the cutis.

It may be true that there is an analogy between the nervous erythism of the first stage of the cachexia thyreopriva and Graves's disease; but if this be so the cause is not evident. For in the one case we have to do with symptoms associated with absence of the thyroid, while in the other we have to do with symptoms associated with the presence of an enlarged thyroid, and actually curable, sometimes, by thyroidectomy. It is possible that irritation of the vagus and sympathetic is a factor common to both cases.

But there are other arguments of greater weight in support of the thyroidal theory of Graves's disease.

In the first place, myxœdema sometimes closely follows Graves's disease, or even, perhaps, accompanies it (Sollier; Von Jaksch, cited by Gauthier; *Clin. Soc. Reports;* my own second case), or the two diseases may occur in different members of the same family (Hadden, Virchow). Above all, thyroidectomy, or other operations on the thyroid, have proved of late years unexpectedly successful in the treatment of Graves's disease. Thus, Lemke has collected thirty-seven cases treated in this way, in all but three or four of which improvement or cure resulted. To this number I can add one case, which is, I think, the first to be reported in this country.

The operation was done by Dr. J. C. Warren, at the Massachusetts General Hospital, three months ago. The patient seems to be steadily, though slowly, improving. The whole gland seemed to have been converted into a firm mass of adenomatous structure, with high cubical epithelium, and, so far as examined, without colloid. (Councilman.)

The probability of a connection of some sort between Graves's disease and myxœdema is made stronger by including the case of acromegalia, which bears a certain likeness to both of the others, presenting the rapid pulse, the tremor, and the sweating of the skin characteristic of Graves's disease; together with trophic changes in the bones and integuments of the head and limbs analogous, perhaps, to those of myxœdema.

On the other hand, the experimental evidence with regard to the cause of Graves's disease, unsatisfactory as it is, favors rather strongly the view that it is due to the injury of certain nervous arrangements; and no theory should pass muster that does not attempt to account

for the extraordinary manner in which practically the whole Graves's disease complex springs almost instantaneously into existence in persons with healthy thyroids under the influence of intense emotion. Sometimes, if the emotion quickly subsides, the symptoms may soon pass away (Gowers. My colleague Dr. F. Coggeshall has seen an exactly parallel case. The patient was a young girl, and the symptoms followed immediately on great excitement attending a whipping, but subsided in a few days.)

My own opinion as regards this complicated matter is that some such statement and explanation as that given by Wette is correct, but may be extended and modified. He thinks that goitre is one of the most important causes of Graves's disease, but not by any means the only cause; that the goitre may excite the cardiac and ocular symptoms, either by direct irritation of fibres of the cervical sympathetic or by indirect irritation of the sympathetic centres; and that many of the general nervous symptoms are due to the action of toxic substances formed by disordered metabolism within the diseased gland.

The explanation which would be most satisfactory is one which would include this, and at the same time cover the cases where Graves's disease comes on without antecedent thyroid disease, and I think that such an explanation can be hinted at if we do not take our physiology too narrowly.

The most probable hypothesis, though it can only be stated with infinite crudeness, seems to me to be as follows:

The Graves's disease complex, in common, probably, with most other neuroses, is the distorted correlative, or caricature, of one or several physiological arrangements (comp. London *Lancet*) in which the nervous system plays the central part. The thyroid has an abundant and mobile circulation, and is supplied with nerves from the vagus and sympathetic. It is thus in position to inhibit (as occasionally seems to occur: see Wette) or to accelerate the heart, and on the other hand it is liable to swell almost like an erectile organ when the heart is acting strongly and its own vasomotor apparatus is weakened. When enlarged, the thyroid, the sympathetic, and the other nerves in its neighborhood thus again act as a centre of disturbance. These results almost certainly occur in many cases of thyroid disease (comp. Wölfler, Wette, and an able paper by Schranz, which I regret my lack of space to cite at length). It is even conceivable that one of the functions of the thyroid in health is to act as a regulatory apparatus for the heart, and it is further conceivable that there is a quasi-physiological connection of the following

sort between the tremor and exophthalmus of Graves's disease, the disordered action of the heart, and the disease of the thyroid:

When a person is suddenly called upon for close attention, he fixes his eyes and holds his breath, his muscles stiffen, and his heart beats faster. If the attention changes to rage or fear the eyes open wider, the heart palpitates, the voice changes, the hand trembles, the face and neck may become turgid from vasomotor paralysis, and even the circulation and secretion of the bowels may become affected.

As calm is restored these symptoms may pass gradually away, but the heart is slow to recover its tone. Judging from the fact that Graves' disease may immediately supervene on such events as this, we may assume as possible that the heart sometimes never recovers its tone, and that the delicate vascular apparatus of the erectile thyroid (which Schranz makes largely responsible for the origin of goitre) is also liable to suffer permanently.

Eventually, nutritive changes may occur (deposition of fats in orbits, etc.); and a morbid complex of symptoms, interdependent and correlated with each other, is formed, and becomes crystallized into what we call a disease.

When any member of this complex is induced, the others are likely, by association, to follow, and a tendency to the complex as a whole may possibly be inherited like a tendency to any other disease, or to a monstrosity. The exciting cause may be any one of many.

Tachycardia without exophthalmus or tremor occurs so frequently with ordinary goitre that it hardly deserves to be called abortive Graves's disease, but it may at least be an analogous affection.

The operation of thyroidectomy in Graves's disease—which, by the way, may be successful when it consists only in the removal of a sarcoma (Tillaux) or a cyst (cited by Gauthier)—may be supposed to act by breaking in upon the vicious circle of influences through which the disease is maintained. The extirpation of a part of the growth usually causes the rest to shrink (Wolff), just as iodine or external cauterization, or electrolysis, or division of the isthmus of the thyroid may cause the same result, and it is probably this and not the reduction of the thryoid secretion by removal of part of its secreting tissue that makes the operation of value. A new set, as it were, is given to the action of the nervous centres, such as more favorable mental surroundings may give, and in favorable cases the old equilibrium is restored. It must not be forgotten that it is just as possible to produce this result from one side as from the other. Absolute

repose for the nervous system, if it can be secured, as it sometimes can, is occasionally as effectual in causing the disappearance of the goitre as the thyroidectomy is in quieting the nervous excitement and the heart.

It is not probable that Graves's disease is related to the functions of the thyroid as a trophic organ, or, at any rate, that it is due to either an increase or a diminution of the normal secretions of the gland. That it is not due to an increase of the normal secretion is demonstrated both by anatomical considerations (coexistence with a small or practically small gland) and by the fact that the myxœdema, which is not compatible with an increased secretion of the thyroid, sometimes follows closely on the heels of Graves's disease, or even accompanies it. Neither can we refer it to a diminution of normal secretion, or we should meet it more often in connection with the involution of the thyroid. Moreover, it has often happened that all the symptoms of Graves's disease have come on with extreme suddenness, in consequence of strong emotion, in persons with normal thyroids, and have again disappeared almost as quickly. Again, it apparently is not cured by preparations of thyroid extract.

It is possible that disordered metabolism, due to a vitiated thyroid secretion, helps to keep up the nervous symptoms of Graves's disease, but this theory is in need of more evidence than it has yet adduced.

Acromegalia probably stands as near to myxœdema and diseases of the thyroid or kindred organs as Graves's disease, if, indeed, the bond be not closer.

It is more distinctly a sort of dystrophy than Graves's disease is, and affects much the same parts that are involved in myxœdema, namely, the bones and integuments of the face and extremities, and eventually, perhaps, of the whole body; for, as Klebs points out, the reason that the ends of the long bones show the growth the most is that the resistance there is least.

The growth of the hair and nails is apt to be impaired in acromegalia, though not to the same extent as in myxœdema, but, on the other hand, the skin often perspires freely, as in Graves's disease. Tremor is also common, and attacks of well-marked palpitation are of frequent occurrence.

In the case of a middle-aged woman, recently under observation in the wards and now in the out-patient department of the Massachusetts General Hospital, I found the pulse one morning 180,

though from her phlegmatic appearance I should not for an instant have expected this. She had, to be sure, taken a dose of thyroid powder two hours previously, but on another occasion when she had not done this I found the pulse 120, and during her stay in the hospital, under the care of Dr. F. C. Shattuck, it ranged from 90 to 100, though she was kept perfectly still.

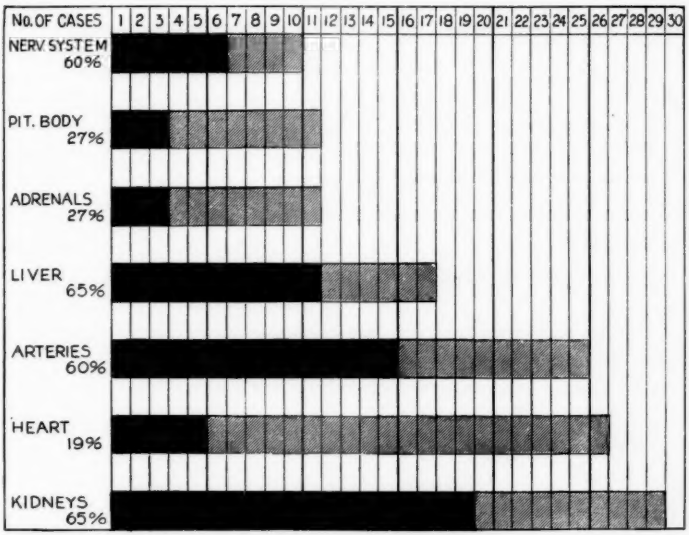
Klebs, who has studied the pathological anatomy of acromegalia quite extensively, explains the rapid pulse on mechanical grounds, believing that the disease originates in an affection of the thymus and that vascular changes occur by which the labor of the heart is increased. It would not be fair for one who is no pathologist to offer a criticism of this theory in detail, but with the tachycardia of Graves's disease before our eyes it would seem more reasonable to seek a physiological than a mechanical explanation, as in the case of Graves's disease. I do not, however, mean to deny the importance of the thymus, or to maintain that acromegalia is distinctly of thyroid origin like myxœdema. I cannot dwell, for want of space, on the recent views of Marie and Marinesco, or on those presented in the monograph of Duchesneau, published in 1892.

Duchesneau calls attention especially to the occasional occurrence of muscular atrophy, but the theory by which he accounts for it, namely, pressure of hyperplastic connective tissue on the nerve roots, is not, I think, the true one. This atrophy is present in a typical form in the case recently at the Massachusetts General Hospital, though without other signs of nerve-root pressure, but so, also, is it present in a case of Graves's disease which I have had the opportunity of studying closely for many years, and in several other reported cases of that kind. The explanation given by Duchesneau would certainly not apply here, and, on the other hand, the occurrence of the atrophy in both these diseases forms another bond of union between them, though its nature is still so obscure.

I have said nothing as yet of disease of the hypophysis in acromegalia, and to save time I present the evidence on that point in the form of a table and diagram.

It is not certain that the dystrophic affections due to thyroid diseases are fully covered by myxœdema and the others that have been mentioned; and in this connection three communications, two by Dr. F. X. Dercum and one by Dr. F. P. Henry, in 1888, 1890, and 1892, are especially important. They describe three interesting cases, characterized by great and widespread hyperplasia of the sub-

cutaneous fat, especially accentuated at certain parts of the body, and attended by pain and muscle-degeneration indicating the presence of neuritis. Perspiration was diminished or absent, and in this and other respects the cases suggested myxœdema. That which makes them especially interesting, however, is that the thyroids of two of the patients, who died while under observation, were indurated and infiltrated with calcareous deposit.



The black portion represents the number of cases in which lesion was found; the shaded portion the number of cases in which the organ is stated to have been normal. In the other cases no statement was made as to the organs. The line at the top gives the number of cases. The percentages are given in round numbers.

The name first suggested for this disease by Dr. Dercum was "A Subcutaneous Connective-tissue Dystrophy of the Arms and Back, Associated with Symptoms resembling Myxœdema." Dr. Frederick P. Henry first described the second of the three cases, and proposed the name "Myxœdematous Dystrophy." Dr. Dercum, in his final communication, says:

"All of these cases lack the peculiar physiognomy, the spade-like hands, the infiltrated skin, the peculiar slowing of speech, and the host of other symptoms found in true myxœdema.

"It would seem, then, that we have here to deal with a connective-tissue

dystrophy, a fatty metamorphosis of various stages of completeness, occurring in separate regions, or, at best, unevenly distributed, and associated with symptoms suggestive of an irregular and fugitive irritation of nerve-trunks, possibly a neuritis. That this, however, does not embrace the whole truth is evidenced by such symptoms as the diminished sweating, the headache, and the contraction of the visual fields noted in Case I.

"Inasmuch as the swelling and the pain are the two most prominent features of the disease, I propose for it the name 'Adiposis Dolorosa.'"

Dr. Dercum further makes the good suggestion that the condition of the thyroid gland should be examined in all cases of obesity. The thyroid is rarely examined as a matter of routine, and least of all microscopically, unless attention is especially called to it, so that our knowledge of the frequency with which this or that change is present, or as to the amount of variation in structure which is compatible with health, is still but slender.

A year ago Dr. F. C. Shattuck was good enough to ask me to see with him a very interesting case which deserves a place in some such category as this, if not indeed a case of myxœdema, though, I believe, the improvement under thyroid treatment has not been very marked, except as regards the condition of the skin. The patient was a lady of about twenty, and the signs and symptoms consisted mainly in an increase in the subcutaneous fat, with changes in the skin not quite suggestive of obesity and somewhat suggestive of myxœdema, a change in the nutrition of the palms and soles, and a marked and peculiar discoloration and brittleness of the nails, associated with an irritability and excitability which finally developed into insanity. I trust that Dr. Shattuck will report the case at greater length.

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A CASE OF LOCAL CATALEPSY; AN UNDESCRIBED HYSTERICAL DISORDER.

By John K. Mitchell, M.D.,
of Philadelphia.

The following very curious case presents, so far as I have been able to discover, an entirely undescribed group of symptoms, so strange and so interesting that it seems worth while to publish it, even as a solitary example. The possible hysterical origin will be discussed after the relation of the history and present condition.

Miss A. B., aged seventeen years, native of Pennsylvania, unmarried, was seen March 28, 1893, when the following history was obtained. Her general health had been excellent until the beginning of the present disease. Menstruation appeared when she was sixteen, and has returned at irregular intervals twice or thrice since, without pain. She is plump, ruddy, and strong-looking. She is not in any way nervous or hysterical, and her habits of life have been good and simple.

About the month of December, 1891, her school-books once or twice fell from the left hand, as if the member were tired and could not retain them. This happened again several times, with intervals of perfect use. There was no pain.

In April, 1892, on the ulnar surface of the third, and on the adjacent side of the little finger of the left hand, there appeared sundry small blisters or blebs containing serum, which caused some itching and came and went several times. In July, of the same year, she received a slight cut with a knife at the root of the left thumb. The hand swelled much; there was aching, redness, and heat. A poultice was applied, and an abscess presently discharged at the site of the cut; there was a good deal of suppuration, and the wound healed slowly in three weeks. All the fingers then gradually became stiff, and have so remained ever since. Other blebs were also formed on both sides of the wrist.

Examination.—The hand is strong, large-boned, of good color, and not wasted in any way. The usual and most comfortable position is with the wrist half extended, that is, in a straight line with the forearm, all the fingers in semi-flexion, the little finger slightly adducted on the palmar surface of the third finger, the thumb in close contact with the palmar surface of the index finger, and all rigidly held like the "lead-pipe" condition. The position of the hand is thus precisely that of the "obstetric attitude."

FIG. 1.

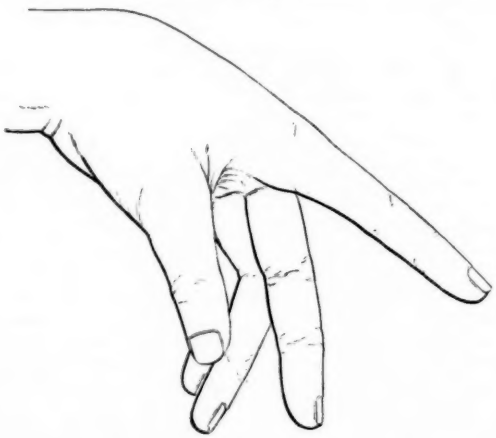
Usual position of the hand at rest.

Slight twitching can be felt in the muscles of the forearm, and in the thenar and hypothenar eminences. All voluntary motions of the wrist are preserved, but none of the fingers. If the wrist be passively and rapidly flexed and extended, the motion, at first easy, soon becomes more difficult, and a similar rigidity to that of the digits possesses it; even then it readily performs voluntary flexion and extension. The fingers may be placed in any position, even the most unusual, and will remain almost indefinitely in the posture thus given; they may be passively

moved with much greater difficulty than would be found in moving the fingers of an ordinarily muscular person against his resistance. The opposition is constant, the stiffness yielding slowly and steadily, not suddenly or with a jerk. Untouched, they continue exactly as placed, like the members of a jointed doll.

The sketch made by Dr. Taylor shows a position in which the hand remained for thirty-eight minutes.

Fig. 2.



At times this rigidity affects the wrist also. The wrist bends best (voluntarily) in flexion, and if the digits are flexed the wrist cannot readily be extended. Whether the fingers are flexed, extended, abducted, or twined about one another, it is with equal resistance, and though, as has been said, they may remain an unlimited time in this position, yet if it be a strained one, and especially if they are in extreme extension, the patient herself places them with the free hand in the semi-flexion of the obstetrical attitude, because the strained extended position causes pain in the wrist.

Sometimes the fingers of themselves pass slowly into extreme abduction, and so remain for a while, gradually returning to what I may call the "normal state" of semi-flexion.

The sense of pain is lost in the whole left hand as high as the annular ligament, where it suddenly becomes acute again. Below this a slight pin-prick does not bleed; there is no sense of touch, localization, or temperature change. There is no tenderness over the nerve tracks in the arm, with this single exception, that there is one minute area of pressure-pain in the middle of the flexor surface of the wrist, just above the annular ligament, over the median nerve's course.

All sensation is perfect on the right hand and arm.

The patient insists that the nails of the affected member have not grown enough in three months to require cutting, but they are not ridged or brittle.

An electrical examination very carefully made at the Infirmary for Nervous Disease revealed no differences of contractility between the two sides.

On a later visit the patient's mother stated that she had particularly noted, as requested, the position of the affected hand during sleep, and found it always rigid in the attitude first described. At Dr. Weir Mitchell's clinic, at the Infirmary, where the patient was sent to be shown to the class, it was noted that the hand was kept forty-one minutes in the strained position in which it was placed, the patient then moving the fingers with the right hand to an easier position.

To help determine the element of hysteria in the case, the girl's eyes were examined by Dr. G. E. de Schweinitz, who reported the result as practically negative. Visual acuity in each eye, 6/7.5; corneal astigmatism according to the rule 0.50 D. in each eye; amplitude of accommodation, 8 D.; insufficiency of the external recti (esophoria), 1 degree; insufficiency of the vertical muscles (right hyperphoria), ½ degree; each optic disk a vertical oval of 90 degrees, more pallid, especially in the deeper layers, than is normal; veins natural in size, arteries in comparison slightly smaller than normal; no pathological changes in retinas or choroid; pupillary reflexes normal; conjunctivæ not insensitive; form fields normal in extent, and in sequence of color appreciation.

There is no pain or tenderness in the spine. Knee-jerk normal. Heart and lungs normal, and all secretions healthy and well performed.

While the general character of the case is analogous to the condition of contracture or rigidity commonly seen in hysterical states, the rigidity is very different from that of the usual hysterical contracture where there is a retention of one fixed position with entire or almost entire immobility. The loss of sensibility is so complete, and the line so abrupt, as to point to an hysterical origin, and the absence of bleeding from pinpricks is a well-known hysterical symptom. Negatively, too, besides the character of the stiffness, there is lack of any evidence of neuritis or of degenerative nerve change, and every nerve of the hand is involved, from the wrist-joint to the finger-tips.

The conclusion must, I think, be that it is hysterical, in spite of the absence of stigmata, mental or physical.

It is difficult to find any name for such a state, which will include or suggest all the symptoms, and it is, I believe, a hitherto undescribed condition. The wax-like or lead-like rigidity maintained in any given position, and the loss of sensibility, remind one of the cataleptic state. Catalepsy, however, is a paroxysmal neurosis; loss of consciousness, partial or complete, attends its manifestations, and in decided cases it is nearly always associated with epileptic or hysterical disease. This patient's local morbid state is unvarying; it is present even in sleep. I have been unable to find anything exactly similar described by any author. Dr. S. Weir Mitchell, Prof. C. K. Mills, and Dr. M. J. Lewis, all of whom examined her, were all of the opinion that the case might properly be held unique. Until some better name shall be found, I have ventured to call it "local catalepsy."

CHLOROMA AND ITS RELATION TO LEUKÆMIA.

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"La publication des faits rares et curieux est toujours chose utile, ne fût-ce que pour indiquer aux médecines une nouvelle cause d'erreur, un nouvel écueil sur lequel leur experience peut faire naufrage. Néanmoins, tant qu'ils sont isolés, les faits de ce genre ne peuvent être considérés que comme des pierres d'attente, et ils réacquièrent de véritable importance que lorsqu'en les rapprochant de faits analogues ou identiques existant déja dans la science, ou peut les faire servir soit à constituer une espèce morbide nouvelle, soit à circonscrire, à délimiter une forme particulière de maladie offrant dans son aspect ou dans sa marche quelque chose de special."—Aran.

Some time ago I had a patient in what seemed to be the last stage of leukæmia. After death the new growths, which differed in their localization from those usually found in leukæmia, had a color so distinctly green, as distinguished from the greenish tint often seen in leukæmia, that the question arose in my mind whether the cases of "chloroma" previously reported were not leukæmic.

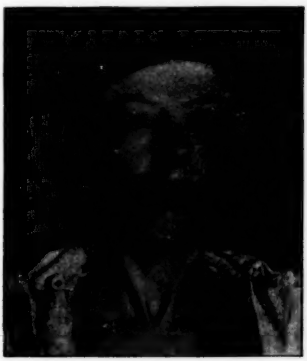
Not knowing that the question had already been raised, I hoped at the best to find in the original descriptions of the cases something bearing out my idea. Soon after beginning researches in the literature I discovered that my idea was not new, but had been expressed by Von Recklinghausen.[1] But, on continuing the search, I found the question by no means settled, and, as the subject has an interest far beyond the peculiar color or the rarity of chloroma, I give the results not only of the study of my own case, but also those of an exhaustive examination of the literature.

My patient was a lad (L. C.) fifteen years and nine months old. His family history, as far back as the grandparents, was without bearing on the case. He had whooping cough at three years, mumps at eleven, measles at thirteen. He never had malaria nor lived in a malarial locality. With the exceptions named, was perfectly well up to the time the present illness began. He went to school until December, 1891, when he was allowed to stay away on account of pains in his eyes while studying. At that time there was nothing abnormal in the appearance of the eyes. About the same time, before Christmas of 1891, the mother noticed that the boy, who had before a good color, was very pale. He was given quinine, presumably as a tonic. Soon after, marked shortness of breath began, with palpitation of the heart on exertion. Even before the end of the year dyspnœa was so marked that the boy "got out of breath after walking to the barn, a distance of 'about a block;' and going back, up a slight ascent, he had to stop at a stile to get his breath." At that time,

[1] Ziegler, in his Lehrbuch, 5. Aufl. i. p. 237, says: "Von Recklinghausen (Tagebl. d. Naturforscherver. in Strassburg, 1885) zählt das Chlorom in die Gruppe der hyperplastischen Lymphome (Leukämie, Pseudoleukämie, multiple Myelome) von der sie eine Spielart darstellen."

i.e., before Christmas, the mother thinks, the boy was as pale as on admission. The dyspnœa continued and became so severe that, two weeks before admission, the patient was given a bedroom on the ground floor, as he could not go up stairs without great discomfort. He never had nose-bleed before this disease came on, but since then has had three attacks, two of them quite severe, so that "he got quite faint." About the end of the year the eyes became prominent. About six weeks before admission swellings appeared in both temporal regions. These were ascribed to injuries, though there was no history of such. For some time the heart's action had been accelerated, and a month before admission exophthalmic goitre was diagnosed. For two weeks before admission the boy had been deaf, and for ten days dizzy.

Status, on admission, March 16, 1892: Undeveloped boy of slight frame; poorly nourished muscles; moderate panniculus. Skin very pale; waxy; no cyanosis; slight œdema on temples, none on the extremities;



a few ecchymoses on thighs, legs, and prepuce, from one to five millimetres in diameter. Infantile sexual organs; no pubic hair. Expression anxious; scleræ bluish, visible mucous membranes very pale. On the teeth, small brownish patches and traces of fresh blood. Small ecchymoses on hard palate and velum; gums very pale, not swollen. Pinching the skin causes bluish-red discoloration, becoming dark yellow by next day. The eyes are prominent; the lids cannot be entirely closed. Above the bulbs one can feel hard masses through the upper lids. These extend from the inner to the outer canthus, are from one-fourth to one-half inch wide, project slightly in advance of the superciliary ridge, with which they form sharp angles. They are immovable, closely fitting the bulbs below, and above giving the impression of growing out from the orbital connective tissue rather than the orbital bones. They have smooth surfaces; the lids over them are dark, freely movable. The eyes project about one-quarter inch beyond the superciliary-malar line. Left pupil smaller than right; reflexes normal on both sides. Ophthalmoscopic examination (Dr. Carrow) shows hemorrhages in both retinæ —small, very numerous, accompanying the vessels; also white patches.

There are symmetrical swellings in both temporal regions, occupying all the space beneath the temporal fascia, and probably half an inch

thick at the thickest part, tapering off to the edges. Owing to œdema in the skin over these swellings it is difficult to examine them. They are smooth and feel as hard as bone. There are no other tumors on the head. The thyroid gland is slightly enlarged. (This must have been of recent occurrence, as the mother had not noticed it, though told to expect it.) There is a fine but distinct thrill, and a systolic murmur over the gland.

Thorax small, but symmetrical. Percussion: right, normal; left, dulness below sixth rib in axillary line, filling Traube's space, and continuous with splenic dulness. Area does not change according to position. Absent vocal fremitus and breath-sounds over it. Respiration 26, costo-abdominal.

Apex-beat in normal position; heart dulness not enlarged; sounds faint but clear; radial pulse 126, small and soft, but regular.

Liver dulness area not enlarged, palpation normal.

Spleen can be felt three fingers' breadth below ribs, moderately hard, not painful.

Percussion over sternum causes pain.

Examination of abdomen negative. For some time there has been nausea, at times vomiting, and a very capricious appetite. The boy has taken little food during the last few weeks.

Urine 1000 c.c.; sp. gr. 1017; acid; yellow. Copious sediment of urates and phosphates, with cylindroids and small hyaline casts. No albumin or sugar. Urea 1.7 per cent.

Blood. Fresh drop shows enormous increase of colorless corpuscles, apparently as numerous as red. Red somewhat diminished, but not otherwise altered. Thoma-Zeiss shows 3,150,000 red and 743,500 white corpuscles to the cubic millimetre; Fleischl, 60 per cent. Dried and stained with eosin and methylene blue, the blood shows great increase of lymphocytes, a few large mononuclear cells with faintly staining nuclei; relatively diminished polynuclear cells, no eosinophile cells; no myelocytes; a few normoblasts.[1]

Three days after admission I made the patient the subject of a clinical lecture in the University Hospital. The diagnosis was leukæmia, based not only on the blood-finding, but also on the history and the other symptoms, viz., pallor, dyspnœa, hemorrhage, rapid heart, gastric disturbance, and eye (retinal) changes. I called attention to the fact that the enlargement of the spleen was hardly sufficient to explain the high degree of leukæmia, and as there was no enlargement of lymph glands I assumed the bone-marrow was extensively diseased. At the same time I pointed out that the blood examination, as far as it had gone, did not confirm this. The pain over the sternum I was not inclined to use as a diagnostic sign of lesion of the bone-marrow. An acute leucocytosis as the result of sarcoma I rejected on account of the long duration of symptoms of blood disease.[2]

[1] Having no preparations ready for the Ehrlich stains we had to forego their use at the time.

[2] My first diagnosis of the case, before taking the history or examining the blood, was sarcoma of orbit (Tenon's capsule) with metastatic growths in the temporal region.

Exophthalmic goitre as a diagnosis fell to the ground as the examination proceeded. The exophthalmus, the goitre, and the heart symptoms were all explicable on other grounds; there was no tremor, no discoloration nor vasomotor change in the skin, no Graefe's nor Stellwag's symptom.

The boy's condition became rapidly worse. The temperature rose to 102° F., pulse between 120 and 180. A trace of albumin appeared in the urine. The goitre and the œdema over temporals subsided, and on the sixth day after admission the patient died. He was able to take only the smallest quantity of food (milk and lime-water, a little rare beef) during the time he was in the hospital. He had a craving for beef.

An autopsy was obtained with great difficulty, and was not complete. For it, and for valuable assistance at it as well as for the photograph from which the illustration is taken, I am indebted to my friend and colleague, Dr. W. J. Herdman. The autopsy notes (condensed) are as follows:

Section—post-mortem. Cadaver of undeveloped and emaciated boy. Marked rigor mortis; very faint discoloration on back. Skin pale, eyelids dark; on thighs and skin of penis small ecchymoses. Moderate panniculus. The periosteum of sternum is thickened and of a pale-greenish color. Omentum well preserved. Mesenteric glands slightly larger and pinker than normal. Slight excess of fluid in peritoneal cavity. Thymus weighs ten grammes, larger part 4 x 5 cm. just above arch of aorta, continuous with a narrow process extending to the cricoid cartilage. Lower part appears normal, not degenerated; upper part is homogeneous and contains a small green tumor. Thyroid not enlarged.

Lungs collapsed; heart in normal position. Left pleura contains 800 c.c. of bloody fluid. Pericardium contains normal amount of fluid; its walls thickened, especially on the left side; of pinkish color, and showing numerous subserous hemorrhages. Heart weighs eight ounces. Over left auricle numerous pale green nodules from one to five millimetres in diameter. Both ventricles contain large, firm, greenish-yellow clots, which are continuous with similar ones in the auricles and pulmonary vessels. Numerous sub-endocardial ecchymoses in both ventricles, especially left. Left lung crepitant over anterior part of upper lobe only; the rest is tough and leathery. Over the posterior part of the lower lobe there is a deposit of greenish material under the pleura and stripping off with it from one to three millimetres thick. Right lung slightly adherent behind, crepitant all over; slight hypostatic congestion in lower lobe posteriorly. The pleura has a deposit of greenish-yellow material in it similar to that in left side.

Spleen slightly enlarged; weighs 150 grammes; capsule wrinkled, of a pale pink color, with greenish shimmer. Cut surface granular, very anæmic, Malpighian bodies indistinct; larger vessels have greenish walls. A small accessory spleen has the same characteristics.

Kidneys, small (4 and 4½ ounces), smooth, very pale; section anæmic, glistening, structure not plain; cortex rather wide; in the boundary zone are numerous small greenish bodies with indistinct outlines. In the pelves small greenish-yellow bodies similar to those on the heart.

Supra-renal bodies appear normal.

Pancreas looks normal, but contains near the tail a pale-greenish body the size of a small pea.

Stomach. Mucous membrane shows thickly-set ecchymoses, especially in lesser curvature, from the size of a pin-hole to that of a pin head; scattered over the mucous membrane are small pale greenish-yellow prominences.

The solitary glands in upper part of ileum slightly enlarged, two Peyer's patches about three feet above valve show shaven-beard appearance. Mucous membrane of colon grayish, the solitary glands black; there are numerous ecchymoses in the mucosa, some in the cæcum being one to two centimetres in diameter.

Liver weighs 40 ounces; capsule smooth, rather cloudy. Under the capsule are a few small pale-yellowish areas. Section shows anæmic glistening surface; tissue soft; acini not distinct; the larger vessels have greenish walls. Cut surface shows a few small, indistinctly outlined, yellowish nodules.

Along the whole length of the vertebral column, from the neck to the pelvis, there is a green, smooth layer under the serous membrane. In the thorax the layer is more than one centimetre thick, and becomes thicker at the insertion of the diaphragm. The mass is continuous with the periosteum, in fact replaces it; the vessels and nerves pass through it. On section it is firm, smooth, in places showing bands of white fibrous tissue, vessels, and nerves. This mass extends on the ribs and intercostal muscles for some distance under the costal pleura. On the abdominal vertebræ it is thin, appearing only as a thickening of the periosteum.

Pericranium thickened and of bright green color. Under the temporal muscles are bright green masses, filling the space between the periosteum and the thinned temporal muscle. Section of the tumors shows homogenous structure, hard and moderately dry.

The dura is greenish, the bone not altered. The walls of all the venous sinuses are thickened and show a green color, like the other parts described, though not quite so bright. The sinuses contain pale-greenish clots.

The brain shows no change beyond extreme anæmia.

On removing the roof of the orbit, the cavity is found filled with a solid green mass, which separates easily from the bone in some places, leaving it smooth. On cutting through the tumor, the bulb is found loose in the front part, the vessels, nerves, and muscles running through the mass. Remains of the periosteum and connective tissue are seen only at the sphenoidal end of the orbit; most of the connective tissue and fat of the orbit is replaced by or converted into the greenish material.

The spinous processes and laminæ of the vertebræ are covered with similar greenish material, the green color passing for some distance into the fibrous tissue running into the dorsal muscles. On opening the spinal canal the dura is found unaltered, but the periosteum is thick and greenish-gray. The most remarkable thing in this part is the transformation of the loose fat of the spinal canal, which is totally converted into soft, greenish masses, some of them several centimetres in length, and having only a loose connection with the dura. Many of these show small reddish areas on section. The cancellated part of the sternum in dif-

ferent places, of the ribs, vertebræ (bodies, spinous processes) and skull, was pale and dry-looking, but apparently healthy; pieces of each were removed for microscopic examination.

For sections, pieces from various organs were hardened in alcohol (95 per cent. and absolute), Fleming, platinum chloride, sublimate, and Mueller's solution. Parts prepared for showing the nuclear structure were hardened by Prof. W. H. Howell, but, owing probably to post-mortem changes, did not give good results. On the whole, pieces hardened in alcohol gave the best results. Sections were cut unimbedded, in celloidin and in paraffin, and stained with alum-carmine, hæmatoxylin and eosine, safranine and *licht-Grün* (Benda), and hæmatoxylin and orange G.[1]

Unimbedded sections were also stained by Gram's method and with methylene blue with negative results so far as bacteria are concerned. Sections were also cut from some of the tissues in Mueller's fluid, the day after the autopsy, on the freezing microtome, and examined in the fluid.

The growth shows the same general characteristics in all parts of the body. It is made up of round or roundish cells, somewhat larger than those of a lymph nodule, which they resemble. They lie in a vascularized reticulum. The reticulum varies in character in different parts of the body, and even in different parts of the same section. In some places it is very fine and in fine meshes, in others the fibres are coarse and the meshes larger. The coarser fibres are evidently fibres of the original connective tissue of the part, as their relations show.

The reticulum showed best in fresh frozen sections with the cells shaken out, and closely resembled that of a lymph gland. Unfortunately, these were not kept, and the drawing made by Dr. Huber, from a hardened section, which was very difficult to pencil, gives a less satisfactory picture than the fresh material. (See Plate: figure A.)

The amount of fibrous tissue varies according to the seat of the growth. Along the vertebræ it is quite extensive, while in the spinal canal there is an extremely fine reticulum with no fibrous septa or bands.

Connective tissue in all places shows a predilection for the new growth.

In the green masses the nerve-sheaths and the adventitia of veins are entirely replaced by lymphoid tissue. The adventitia of arteries is involved, though less completely.

The vascular supply of the growths is usually extensive, and consists of vessels of old and new formation. The arteries seem to be those of the original tissue, but the accompanying veins are often so involved in the growth, and their lumen so altered by growths in their walls, that it is difficult to recognize them. There are, besides many vessels having only an endothelial lining and a thin fibrous, or probably, in some cases, muscular wall, the latter closely surrounded by the new growth. Lymphatic vessels are numerous and in many places show dilatations, or open out of cystic cavities filled with colorless corpuscles, and some-

[1] Paraffin sections were stained by Dr. G. C. Huber, assistant professor of histology, by the two latter-named methods, but no mitoses could be found. Dr. Howell intended to study the pieces from the point of view of blood formation. As this was prevented by his change of location, Dr. Huber kindly took up that part of the subject, but with negative results, though he devoted an amount of time and care to the matter that can only be appreciated by those who have done similar work.

times containing a small proportion of red blood cells. Some of the cavities are as much as two to three millimetres in diameter, lined by endothelial cells and filled with cells like the others described.

The cells, as mentioned above, are round, or sometimes longish, but never spindle-shaped. They have a small amount of protoplasm—in places almost none; in others, especially in the denser connective tissue, the nucleus occupies about two-thirds the diameter, with finely granular protoplasm around it. The cells in the growth do not differ in their appearance from those in the bloodvessels. They show no evidence of degeneration. Spindle cells are found only along the vessels. "Mastzellen" appear in excessive numbers in various organs in or near the new growths.

The topographical and other peculiarities of the growths not yet described can best be studied in connection with the different tissues examined.

In the orbit the growth extends from the bony walls to the bulb and eyelids, and involves all structures but the optic nerve and bulb. The periosteum shows, to the naked eye, only in the posterior part, but microscopically it can be seen that the inner (bone) layer is not at all infiltrated. In some places the bone separates easily, in others it is closely adherent (decalcified sections). A few fat cells are left in the mass, but almost all the fat and connective tissue is replaced by lymphoid tissue. The nerves lie in masses of the tumor without any trace of their sheaths. The adventitiæ of the smaller arteries and of the veins have disappeared. The sheaths of the muscles in many places are replaced by the new growth, and in many places there is round-celled infiltration between the bundles of muscle fibres. In many cases the intra-muscular septa are infiltrated, while the sheath at the same level is not involved.

The growths in the dura and sinus longitudinalis are also developed from the external layer of the membrane (as is the case in all parts). The microscopic appearance of the dural tumors is rather different from that found in other parts, in the greater amount of connective tissue. This is so arranged as to give a slightly fasciculated appearance. In many places there are long narrow spaces between lines of hard fibrous tissue, filled with round cells, and causing an appearance similar to that in inflammations in fibrous tissue, or in the infiltration around a carcinoma or the wall of an old cavity. The vascular supply of the tumors in the dura is very much less than in other situations.

The thick masses along the bodies of the vertebræ resemble those of the dura in the frequent appearance of a fasciculated arrangement. In the middle of the mass this resembles carcinomatous structure, though the cells are of the same lymphoid form as in other places. The alveolar-looking part is inconsiderable, and around it the tissue has a lymphoid appearance, varied according to the bands of original connective tissue, vessels, and nerves running through it. Nerve-sheaths and adventitiæ are entirely replaced by lymphoid tissue. In many places the walls of the veins are filled with round cells, so that the lumen appears only as a narrow Y-shaped slit. Channels and irregular cavities lined by endothelial cells and containing cells like those of the new growths are numerous. In the loose connective tissue between the dense mass and the pleura there are scattered groups of cells, less numerous and smaller near the pleura.

The pleura is extensively involved, so that it is difficult to find places

where there is no round-celled infiltration. In some parts this causes thickenings visible to the naked eye. These have the same structure as in other parts. Often there is an abrupt boundary between lung and new growth, but in other places the lymphoid tissue passes into the lung, replacing it more or less completely. The borders of the infiltration are not well defined, the septa being thickened for some distance around the denser infiltrate by numerous round cells. In some parts, in the vicinity of the new growths, there are catarrhal, œdematous, and hemorrhagic areas.

The growth in the temporal region shows very interesting relations. It is confined between the deep layer of the pericranial and the temporal fascia and muscle. Beginning at the upper border as a narrow layer between the two membranes, it becomes thicker toward the middle of the muscle, where it reaches a thickness, in the hardened specimen, of 1 cm. Nearer the inner surface the growth is without trace of muscle fibres. Farther away from the bone isolated fibres are encountered, very narrow, but still showing transverse striæ, and nuclei which stain well. These are separated by lymphoid tissue, but still farther away the fibres are closer together. Finally, just under the temporal fascia, is a layer of muscle fibres 1 mm. thick, with very little infiltration, but with an excessive amount of connective tissue, as if many fibres had disappeared. The new growth has a fine reticulum. Spindle cells are rare. The vessels exhibit the same characteristics as described in other parts.

On the spinous processes the periosteum shows no infiltration close to the bone. The fibrous origins of the dorsal muscles are densely packed with lymphoid cells, sometimes extending far out between the muscles (at least 1 cm. from the bone). The walls of the vessels are infiltrated in many places.

The lymphatic glands examined were those from the mesentery, the only ones which showed enlargement. These show marked hyperplasia. The medullary sinuses are not to be recognized as such, being uniformly filled with cells like those in the nodules, but not quite so closely packed. The fibrous septa and reticulum are not hypertrophied.

The spleen shows areas of lymphoid hyperplasia which pass gradually into tissue that is almost normal. The hyperplastic areas are sometimes as much as 5 mm. in diameter. These, like the similar change in the lymph glands, cannot be distinguished from those in sections of the same organs from cases of leukæmia.

The larger mass of the thymus shows only a slight infiltration of lymphoid cells in the septa and an increase of cells in the central parts of the nodules. The long narrow process extending up to the cricoid is made up of a narrow strip of almost normal tissue, passing abruptly into lymphoid material which shows no trace of the original relations. The extremity of the process, which contained a small greenish tumor, has a very thin capsule but no septa. The peripheral part is made up of lymphoid tissue of uniform structure. The tumor can be recognized by its closely packed cells, which lie in a fine reticulum. This central part lies loosely in an irregular cavity, the borders of which are formed by lobular masses the size and shape of thymus nodules. In some places the two parts have no connection, but in others the tumor passes into the adjacent structure. In the central part, and in the extreme periphery of the gland, the cells are round, but in a narrow zone at the

edge of the cavity described, the cells are long and lie in long, narrow spaces between fine lines of fibrous tissue. There are a few Hassall's bodies in the peripheral part. In other words, all the fibrous tissue of this part of the thymus has undergone lymphoid change. In all parts dilated lymph channels and cystic spaces filled with lymphoid cells occur.

Numerous sections of the bone-marrow were stained and examined by Dr. Huber with negative results. In some places there seems to be an increase of lymphoid cells, but after careful examination I think Dr. Huber's idea that these are in the vessels is correct.

The liver shows a scanty infiltration of lymphoid cells in various parts, without definite relation to the zones of the acini. In some places the cells are more closely aggregated around the central vein, in others in the portal areas, especially in the connective tissue and the walls of the portal vein. In some places small lymphomatous areas occur. These are not sharply circumscribed. At their magins the capillaries are dilated and filled with (leukæmic) blood. Farther in, no liver cells are to be seen, the original tissue being replaced by the lymphoid growth.

In the kidneys the epithelial cells, including nuclei, are well preserved. In the boundary zone or the pyramid near it are a few lymphoid areas, not more than 3 mm. in diameter. The smaller ones are mere diffuse infiltrations. The larger ones show masses of lymphoid tissue between the tubules. The parts of the tubules between the new tissue appear normal, but at the sides the tubules are compressed and their cells atrophied. In the cells of the branches (especially ascending) of Henle's loops, also perhaps in the collecting-tubes, in the pyramids, are fine greenish-yellow, glistening granules, sometimes scattered, sometimes in small masses. Rarely, yellow granules are seen in the intertubular tissue. The yellow pigment occurs in only in a few places, and apparently has no relation with the infiltrations. The parts sectioned show no hemorrhages.

The supra-renal bodies are normal. In the fat around them the walls of the vessels show round-celled infiltration. In the stomach there is an unusual quantity of lymphoid tissue at the base of the tubules. In many places the intertubular tissue contains an excess of small cells, and in some places, just beneath the surface, these cells form large masses extending over areas of several millimetres.

The most obvious features of the case are those relating to the tumor-formation, and they relegate it at once to the category of chloroma as described by systematic writers. (See the works of Birch-Hirschfeld, Ziegler, and Klebs.)

The first mention I can find of a case of this kind is by Allan Burns (*Observations on the Surgical Anatomy of the Head and Neck.* By Allan Burns. 1st Am. ed., Baltimore, 1823, p. 386). The history of the case is not given in full.

The patient was a young man who had a tumor in the left orbit, with protrusion of the eye, followed by loss of vision and destruction of the eye. Later a similar growth appeared in the right orbit. The patient had paralysis of the lower extremities and bladder and died about three months after the beginning of the disease.

After death, tumors were found in the orbits which were supposed to have grown from the lachrymal glands. At all events those glands were diseased. There were tumors on the frontal bone, in the frontal, ethmoidal, and sphenoidal sinuses, the nose and the dura mater, with thickening of the periosteum and dura, caused by deposits of a peculiar greenish-yellow substance having a cartilaginous hardness and containing more or less fibrous tissue.

Burns thought the disease one *sui generis*. "The series of parts affected and the mode of propagation were different from what is generally met with in fungus hematodes or medullary sarcoma."

The next case was reported by Balfour (*Edin. Med. and Surg. Journ.*, 1835, xliii. p. 319), of Edinburgh, in 1834, as one of peculiar disease of the skull and dura mater.

In 1836, Durand-Fardel (*Journ. hebd. des Prog. des Sci. Méd.*, Paris, 1836, t. iii. p. 207) reported a case. He cited the case of Balfour, the only similar one known to him, but said there was a third observation of the same kind in the *Revue d'Edimbourg*. It was impossible for him, as it has been for me, to find an account of it.

Dittrich, of Prague (*Prag. Vierteljahrsschrift f. die prakt. Heilk.*, 1846, Bd. ii. p. 104), in 1846, at the autopsy of a woman who died with symptoms of scorbutus, found "dirty green" tumors on the periosteum of the vertebræ, ribs, and cranium, and also in the kidneys and ovaries.

In 1853, King (*Monthly Journ. of Med. Sci.*, Edin., August, 1853, vol. xvii. p. 97), of Glasgow, under the title of "A Case of Chloroma," reported the details of a case seen in 1849, having symptoms much like those in my own, but with the tumors limited to the head. Models and preparations of this case were placed in the Museum of Anatomy in the University of Glasgow.

In 1854, Aran (*Arch. gén. de Méd.*, 5. sér., 1854, t. iv. p. 385) reported a case seen in 1851, and made it, with the cases of Balfour, Durand-Fardel and King, the subject of an anatomical and clinical study. The same case was published by Lebert, who made the microscopic examination, in his *Traité d'Anatomie Pathologique* (Paris, 1857, i. 323, plate xlv., figs. 1 to 4), with illustrations of the growths. These two articles served to call attention to the subject and form the first landmark in its literature. It seems proper here to correct a wrong impression concerning the name chloroma. Most of the German writers, following Huber, speak of Aran as the author of the name. But King's article, with the word in the title, appeared fourteen months before that of Aran. The latter distinctly says (*loc. cit.*, p. 386): "M. King, a publié dans un journal Anglais, en lui donnant le nom de chloroma," etc. Aran gave "cancer-vert" as the synonym for chloroma. It is not a little curious that King does not use the name in the

body of his paper, so seeming to indicate that it was already in use, but I can find no previous application of the term.

Mackenzie (*A Practical Treatise on the Diseases of the Eye*, by Wm. Mackenzie, M.D., Philadelphia, 1855) at least as early as 1855 had a section on chloroma in his chapter on the Diseases of the Lachrymal Glands, and cited a characteristic case seen by himself in the Glasgow Eye Infirmary in 1830–'31. Mackenzie spoke of a similar case reported by Williams (*Med. Gaz.*, London, 1849, xliv. p. 854. See also *Path. Trans.*, ii.). A careful study of the latter makes it certain it was not one of chloroma, and the same remark is true of the cases of Sir E. Home, referred to in another place (*loc. cit.*, p. 970) by Mackenzie.

In 1855, Hillier (*Trans. Path. Soc. of London*, 1855, vii. p. 337) reported a case to the London Pathological Society. This is spoken of as a case of recurrent tumor of the orbit, and its resemblance to the chloroma of Mackenzie mentioned.

In 1866, Dressler (*Arch. f. path. Anat.*, etc., 1866, Bd. xxxv. p. 605) described a case of the same kind in a letter to Virchow. The case occurred in 1860, in Prague. Dressler was not aware of the case of Dittrich.

No other example was seen, apparently, after that until 1878, when the occurrence of an example in Thiersch's clinic gave the late Carl Huber an opportunity for a thorough anatomical and clinical study of all the cases known to him. (*Arch. der Heilkunde*, 1878, xix. p. 129.)

Since then instances have been more frequently observed. In 1882, Behring and Wicherkiewicz (*Berlin. klin. Wochenschrift*, 1882, No. 33, p. 509) reported one from Posen; Waldstein (*Arch. f. path. Anat.*, Bd. xci. p. 12) one from Heidelberg in 1883 (in this case leukæmia appeared late in the disease). In the same year Chiari (*Prag. Zeitschr. f. Heilk.*, 1883, Bd. iv. p. 177) reported a third case in Prague. In 1884, Gade *Nord. Med. Arkiv*, Bd. xvi. No. 19, and *Comptes-rendus*, xvi., No. 22, p. 20) reported a new case with an analysis of the cases known to him, ten in number. The year after, Von Recklinghausen (*loc. cit.*) mentioned he had seen a case, and raised the question of the leukæmic nature of chloroma. Finally, Höring (*Arbeiten aus d. Path. Anat. Inst. zu Tübingen*, Bd. i. Heft 1, p. 180), in 1891, reported a case from the Tübingen clinic.

My own case raises the total to seventeen, those of Burns, Mackenzie, and Hillier having been overlooked before. There are, perhaps, cases recorded not published. Hamilton in his *Text-book*, says (i. p. 506): "The author has several times met with a peculiar soft, light green-colored tumor, situated in the anterior mediastinum, usually attached to the posterior aspect of the sternum. It had all the appearance [microscopic?—D.] of a round-cell sarcoma, but had a quite remarkable

green color (chloroma)." Unfortunately no other particulars are given (I shall mention later cases that are either the same as or closely related to chloroma).

In all the cases the most obvious point in common is the peculiar color, which suggested the name chloroma or cancer-vert. The precise tint was probably not the same, making due allowance for difference in nomenclature. Thus, Burns makes it "greenish-yellow;" Balfour, "bright olive green;" Durand-Fardel, "vert pomme très foncée;" Dittrich, "dirty-greenish;" King, "yellowish-green" (his plate shows a dark green); Aran, "gris-verdâtre" or "gris-vert;" Mackenzie, "light greenish or whey color;" Hillier, "yellowish green;" Dressler, "light green;" Huber, "dark yellowish-green;" or, in fresh (operation) specimens, "exquisite light yellowish-green;" Behring and Wicherkiewicz, "beautiful dark grass-green;" Waldstein, "pea-green or darker;" Chiari, "light green;" Gade, "vert-jaunâtre to vert-grisâtre;" Höring, "yellow or greenish-yellow," or "ziemlich reines grün." In my own case the color could be best described as pea-green. It was much like the tint shown in the plates of Chiari and Dressler; not so dark as King's or Lebert's. It differed, however, in various parts, so that some were pale sage-green, others darker, or again with pink, brown, or red stains. The small growths in the liver and kidneys were almost white, but in the pancreas and thymus the color was distinctly green, though pale. The color gradually faded from the preserved specimens. Owing to the fact that the solutions were frequently changed, it is impossible to tell whether the color was dissolved out or bleached.

The cause of the color still remains unknown. Balfour, without making any examinations, supposed it to be due to some pigment allied to bile coloring matter. Dittrich attributed it to putrefaction, which was plausible, though in my case, as well as in some others, as also in the parts removed during life in Huber's case, such an explanation is impossible. King had part of the tumor and the spirit in which the specimens were kept examined by Dr. R. D. Thompson, who reported that "he could find no trace of bile, the only source from which green coloring matter could emanate in the human system so far as we know at present." He quoted the opinion of Lebert, that a greenish color could arise from a local infiltration of a peculiar kind of fat. (Lebert, *Physiol. Pathologique*, ii. p. 122). King also speculated as to the possibility of the color being due to the altered extravasated blood, but noted that old and recent tumors had the same shade of green. Aran and Lebert did not venture to explain the nature of the coloring matter. Virchow, in his comments on Dressler's case, said the color was diffused in the tissue without granular or crystalline deposits. This was in tissue which had been dried, so that the conditions were different from those

in other cases. Huber was the first to make careful investigations into the nature of the color. Without describing his methods in detail, suffice it to say that he ascribed the color to certain fine molecules found in the cells, which he thought were allied to, if not really fat. This opinion was shared by Chiari on account of the reaction of the granules seen by him to alcohol and ether and to osmic acid. Chiari says, and the explanation is plausible, that in Huber's case the granules were so small as to be recognized with difficulty. In his own this was not so, and the recognition of the fatty nature of the granules was easy. Chemical examinations by Huppert proved the coloring matter to be one hitherto unknown in the human organism. Höring came to conclusions identical with those of Chiari. Behring and Wicherkiewicz claimed to find in the tumors in their case an unusual proportion of chlorine. They were led to make the analysis from having found that tough sputum containing many desquamated cells and inspissated pus when treated with chlorine became grass-green.

Waldstein thought the coloring matter a derivative of blood. From Langhans's experiments (*Arch. f. path. Anat.*, Bd. xlix. p. 102 *et seq.*) it might be supposed that the color was due to altered extravasated blood. The following facts oppose this: The green color under the microscope is not so distinct as Langhans described it; it occurs often when there is no other sign of old extravasation; in parts (spinal fat, intestines) with numerous extravasations there is neither more nor less color than in other places, except red stains from orange-red granules, which occur in the altered spinal fat. Examinations by Otto in Gade's case showed an absence of both bile and blood-coloring matter, so that Gade shared the opinion of Chiari and Huber, that the color was dependent on fatty granules. Opposed to this view, and impossible to reconcile at present, are the negative results Von Recklinghausen had by the use of osmic acid. The latter held that the color was a parenchymatous one. He compared it, as did Huber and Dressler, with that of old pus, making this one of his reasons for believing the color parenchymatous (as Virchow had done).

Not knowing at the time the difference of opinion, I lost an opportunity for having examinations made by an expert. The idea I had from the literature, that the pigment was of a fatty nature, seemed confirmed by the abundant, highly refracting granules which were certainly present in the cells in the fresh frozen sections. In sections examined later, after the tissue was decolorized, the granules were absent. I also thought that the peculiar color was simply an exaggeration of the greenish tint so common in the blood-clots and the neoplasms of leukæmia. The finding of greenish-yellow pigment in the renal epithelium in Chiari's case and my own seems to me to oppose the idea that these were fatty, since in my own case, though the green tumors have long been bleached, sections

of the kidney from specimens more than a year in absolute alcohol show as much pigment as ever. The pigment must be altered in some way in the kidneys, if it be really the same as that which gave color to the fresh specimens. Our knowledge of such pigments is so imperfect that the whole subject must be left to future investigations.

In other physical characteristics, the chloromatous tumors exhibit points of resemblance. The consistency varies from a gelatinous or soft elastic (Aran) to a firm cartilaginous (Balfour, Burns). Most frequently it is described as moderately firm or brawny (Dittrich, Höring, Huber).

In my own case, I could find all the different degrees of hardness, from a soft elastic in the orbit, or very soft and gelatinous in the spinal canal, to dense cartilaginous hardness along the vertebræ.

The cut surface is described by various writers as homogeneous, with or without fibrous septa, depending on the seat; and this, too, was to be seen in my case.

In some cases, a turbid greenish juice could be produced by scraping the cut surface (Aran); in others the juice was scanty and colorless (Huber), or thick and creamy (Dittrich), or the tissue was almost dry (Höring). These characteristics, as also the presence of a moist lustre (Behring and Wicherkiewicz, Huber), depend on the seat of the growth and the firmness and vascularity of the tissue in which it develops. In my case the tissue in the orbit, more so that in the spinal canal, was moist and yielded much juice, that along the vertebræ and on the pleura was almost dry.

The external surfaces of the tumors were smooth or nodular—tumors proper, as distinguished from uniform infiltrations, being usually nodular.

In regard to the seat of the growths, we find most interesting data. In all the cases reported some part of the head was affected. In twelve cases the scalp contained greenish deposits; in fifteen the dura, in thirteen the orbit, in eleven, various parts of the periosteum of the face. Less frequently we find the green substance in the periosteum of the vertebræ and the ribs adjacent (five cases); under the temporal muscle (five); bone-marrow (four); liver (four); kidneys (eight); spleen (three); mesenteric glands, stomach, intestines, pleura, lungs, heart and pericardium, mediastinum, submaxillary and cervical lymph glands, nares, pharynx, testes, ovaries, prostate, lingual tonsil, bronchial lymph glands, pancreas, thymus, pelvic connective tissue, broad ligament, skin, mammary gland, internal and external ears, in eye at insertion of optic nerve. (In several cases the examinations were not complete.)

The marked predilection of the periosteum, especially that of the head, has been noticed by all observers, and most of them look on some part of the periosteum of the head or face as the starting-point. So Huber, in whose case tumors were first noticed in the mammary gland, believed the primary disease was in the head. It does not seem possible, either from

the histories or post-mortem records, to show a common point of origin, as in the orbit. Burns thought the disease primary in the lachrymal gland. Mackenzie examined King's specimens, and concluded, as did King, that the disease began in the periosteum of the lachrymal fossa, affecting the gland secondarily.

The predilection is not for periosteum alone, but for fibrous tissue in general, as strikingly exhibited in my own case.

In regard to the histological structure of the growths, we must bear in mind the fact that we cannot accept without criticism the names given by writers of more than a generation ago, for we know, from what has been said, that the growths belong to a class which has been the subject of endless controversy and change of name. Interesting as it would be to quote the histological descriptions of different writers on the subject, the recital would carry this paper to an inordinate length, and the necessity is less urgent from the fact that the recent literature is easily accessible.

The new growths are sarcomatous, in the sense that they are "connective tissue formations, with excessive development of the cellular elements." (Virchow, *Path. Geschwülste*, ii. p. 177.) Taking the most obvious view, that they are periosteal sarcomata (metastatic periosteal sarcoma, Huber), we find certain points of difference from the usual conditions in such tumors.

There is an absence of bone formation. It is true, some of the older writers (King, Aran) mention spicules of bone in the tumors. But these were found only when the bone was usured, and the process was probably more like that which occurs in many diseases affecting the nutrition of the bone than that which takes place in myelogenic sarcoma.

There is an absence of polynuclear giant cells, so common in periosteal sarcoma. The cells found in different cases agree closely in size, shape, and appearance.[1]

The difference between the myelogenic form of periosteal sarcoma and chloroma can best be explained by the fact that the latter develops from the outer layer of the membrane. Lücke[2] has, indeed, figured a periosteal sarcoma having a lymphoid structure, but it is not identical with the growths we are considering.

Again, chloroma differs from other forms of periosteal sarcoma in the absence of a tendency to form fibro-sarcomatous structure. The

[1] Although a minor point, it seems necessary to speak of an apparent contradiction to the above statement. Virchow (Path. Geschw., ii. p. 220) says that Lebert (loc. cit.) "pictured large polynuclear cells ('grosse vielkernige zellen,')" etc. Lebert certainly has a figure (4) which looks something like a giant cell. In the text, however, he says the cells measured from 10 to 20 mm. in diameter, and nowhere mentions polynuclear giant cells. The figure, therefore, represents a number of cells.

[2] Die Lehre von den Geschwülsten, etc. Pitha-Billroth's Handbuch, p. 196.

only descriptions that seem to contradict this statement come from the earlier days of less exact technique. In scrapings the spindle cells and original fibrous tissue would be more striking than in sections. The fibrous tissue in all cases carefully examined was that of the original tissue.

In view, however, of certain clinical features observed in cases of chloroma, but even more so on account of the tendency of pathological knowledge, we must go beyond the diagnosis of sarcoma, since this has long been a collective name, including neoplasms of the most diverse kinds. We must make an attempt at a more distinctive histological classification, and must endeavor to learn something of the nosological and etiological relations of the growth. The latter is of the greatest importance, for we know that on the ground of causation we have separated a number of diseases from the category of sarcoma.

As regards the first point, my studies lead me to coincide with Von Recklinghausen[1] as to the lymphomatous structure of the growths. Höring, Chiari, and Behring, and Wicherkiewicz, all describe the tumors as lymphomatous in structure. Huber, too, described the tumors in his case as made up of cells lying in a network similar to that of the lymph glands, but not so regular and delicate.

Waldstein, who was led by the clinical features of his case to look at it from a new standpoint, called the growth chlorolymphoma, and declined to consider it a sarcoma. In some respects Waldstein went too far. Thus, he rejected the idea of sarcoma especially on account of the structure of the tissue, and the fact that nowhere else in the body could secondary tumors be found. So far as the statement regarding the structure is concerned, it is impossible to understand it literally. The assertion in regard to metastases seems strange in the light of Waldstein's description of greenish-colored lymph glands ("zwar nicht wesentlich vergrössert,") in the porta and behind the stomach, and a greenish discoloration of the dura and inner surface of the cranium, not to mention a walnut-sized green mass in the mediastinum. Waldstein, however, explained all this by saying the tumor was simply a hyperplastic lymph-gland, and the color due to numerous small and large hemorrhages. He thought the discoloration of the dura and the bone marrow could be explained by the fact that during life the urine was green-colored, though why the discolorations were so localized he did not explain. The peculiar fact about the urine is interesting in connection with the finding, in Chiari's case and my own, of a peculiar pigment in

[1] Von Recklinghausen said (loc. cit.): "More important than the green color is the pure lymphomatous structure, which appears in all the cases reported. Besides this is the multiple appearance of the growths noted in all except the imperfectly reported cases, and the distribution over the larger part of the tissue which stands in most intimate relation to the lymph system."

the kidneys. In my case the urine did not have a greenish tint, nor did it show any peculiar color reactions.

Höring has criticised Von Recklinghausen for saying that the lymphomatous character of the tumors was made out in all cases of chloroma, and says this cannot be accepted in the face of the belief of Virchow, Huber, and Chiari that the tissue was sarcomatous. If that were good reasoning we should have to call Aran's tumors "cancer," Hillier's "fibro-cellular," etc. It is most unfortunate that Virchow could examine the specimens only after they had been dried for years. Almost three years elapsed between the time when Virchow referred to Lebert's case and that of his examination of Dressler's specimens, and from the remarks appended to Dressler's letter it does not appear that Virchow recalled the "famous case" of Aran (*Path. Geschw.*, ii. p. 220).

Not only from later authors do we find various reasons for assuming the lymphomatous character of chloroma, but, as far as we could expect, from earlier ones also. King, for example, says the tumors showed a mass of irregular granules, some of a round, others of an oblong shape, mingled with imperfect fibres or fine filaments.[1]

Aran's and Lebert's descriptions prove that their growth had a structure identical with the others.

Hillier described the tumor as a combination of the fibro-cellular and fibro-plastic. In other early cases, although we have no microscopic examinations to depend on, the other features of the tumors agree so closely that we have every right to view the growths as Von Recklinghausen did.

The idea that other forms of tumor may have the characteristic color of chloroma cannot be said to be groundless, but so far we can say that all the cases described as chloromatous agreed histologically. The remarkable case of Bock (*Arch. f. path. Anat.*, Bd. xci. p. 442) forms, I believe, a unique exception to the above statement. In that case the green color was due to biliverdin. The growth was adenomatous, though Bock called it sarcomatous simply because it was anomalous. The case evidently has little right to the term "chlorom," given in the "register" of the journal in which it was published.

The tumors can best be described, I think, as lymphomata, in the original sense (Virchow, *Path. Geschw.*, ii. p. 563). This seems less likely to lead to misunderstanding than terms like lympho-sarcoma or lymph-adenoma.

The lymphoid structure of the tumors is the principal thing in making the distinction, for although the similarity of lymphoma and lympho-sarcoma, histologically, is increased by the finding (Arnold, *Arch. f.*

[1] A criticism of King's description by Huber is based on a misconception of the word "areolar" in the then commonly used sense of connective tissue. Huber supposed it to indicate an alveolar arrangement ("areolares Gefüge").

path. Anat., Bd. xcviii. p. 506; Ribbert, *Ib.*, Bd. cii. p. 452; Klebs, *Allg. Path.*, ii. p. 673) of giant cells in simple hyperplastic lymph glands and lymphomata, their absence, as in chloroma, I look on as a point to be observed in the differentiation. This, of course, may not be a constant feature of chloroma, but, like all other distinguishing points between the two forms in question, becomes of use in cases lying at the extremes.

But for the present I think we cannot do better than continue to use the term "chloroma," and some synonym, as lymphoma, lymph-adenoma, lympho-sarcoma, or myeloma, could be used to express peculiar features or the views of the reporter.

In endeavoring to classify a tumor of this kind we have a striking evidence that the histological structure is not enough. It would be a waste of time to bring up other examples to illustrate this statement. What is necessary to complete our knowledge is the establishment of the etiological relationship of the growth. So far, attempts to solve this have been fruitless. In the meantime we can perhaps increase the chances of improving our outlook by examining the clinical characteristics of the cases.

The analysis of the cases I have gathered agrees in the main with those of Huber and Gade; but on account of the larger number of cases, as well as some features I wish to emphasize, I give my results.

Chloroma is most frequent in early life—the average age of fifteen cases being 15.26 years. Another is described as a young man (Burns); Von Recklinghausen does not give the age in his case. The youngest was four years old (Dressler); and seven were under eight. But that the disease is not limited to the very young, follows from the fact that five were over twenty, one twenty-eight, and one forty-four years (Waldstein).

In six cases females were affected; males in ten.

The course of the disease is short. The average duration in twelve cases in which it is given is five months. In one (Balfour) the patient is said to have been sick for two or three years, but active symptoms were observed only during a few months. But although in many cases the course of the disease was brief, in that of Durand-Fardel the patient was sick two years, having very abundant hemorrhages for eighteen months. In my own case I have used three months in making the table, but here, as in Balfour's case, the course must have been longer.

Exciting causes are rarely given. In Chiari's case the disease began with toothache, and the tumor first appeared in the site of the extracted tooth.

The fact that three cases were observed in Prague, three in Glasgow, and two in Paris seems worth noting.

The family and previous histories were usually good. Balfour noted, however, a phthisical family history; Hillier's patient was delicate, and

Durand-Fardel's was of lymphatic temperament, and sick four years with frequent catarrhs and hemoptysis.

Early symptoms were as follows: Pallor, 6 cases; emaciation, 3; nose-bleed, 3; "scorbutus," 1; petechiæ, 1; loss of energy, 2; fever, 1; frequent pulse, 3; headache, 3; tinnitus aurium, 2; deafness, 7; double vision, 1; loss of vision, 2; exophthalmus, 6; facial paralysis, 2; feeling of oppression, 1; prominence of temples, tumor of mammary, feeling of constriction, toothache, each 1. (Many cases were treated in eye or surgical clinics, and only the special histories are available.)

Symptoms occurring later are: Thirst, fatigue, strabismus, double vision (in addition to those noted before), deafness, otorrhœa, pain in epigastrium, dyspnœa, abscesses, anemia, œdema, hemorrhages from lungs, intestines, in skin, and from the nose, obstruction of the nose, fever, frequent pulse, nephritis, irritability, coma, delirium, convulsions, wasting, constipation, vomiting, involuntary stools, diarrhœa, anorexia, pain in the region of the liver, craving for meat (King, Dock), disgust for meat (Aran), enlargement of spleen (two, probably four, cases), swelling of thyroid.

Death usually occurred from profound exhaustion, inability to take food, and often with some of the nervous symptoms mentioned above.

This brief synopsis shows the great resemblance, clinically, of chloroma and leukæmia and pseudo-leukæmia. It is not within the scope of the present paper to consider at length the relations of leukæmia and pseudo-leukæmia. A great deal of valuable work has been done on the subject in the past few years, with the result of showing that certain cases of so-called pseudo-leukæmia represent an early ("aleukæmic") stage of leukæmia. All of them await the discovery of the etiological factor to make their relations clear. (Without wishing to make invidious distinctions, I refer to papers of Dreschfeld, *British Medical Journal*, April 30, 1892, p. 893; *Deutsche med. Woch.*, 1891, No. 42, p. 1176; Westphal, A. D., *Arch. f. klin. Med.*, Bd. li., Heft 1; editorial, *Medical News*, Phila., February 18, 1893, p. 191.)

It is necessary, however, to consider certain features of the cases before claiming more than a resemblance between the diseases named. I refer to deafness, exophthalmus, and the condition of the blood, for the other symptoms are common to many processes, the differential diagnosis of which is quite unnecessary.

As explanations of the deafness noted so often, in the cases of Durand-Fardel, Aran, Behring and Wicherkiewicz, and Gade, greenish masses were found in various parts of the internal or middle ear, in several others in the external auditory canal. In other cases the ears were not examined.

Deafness has been noted in leukæmia, and although in some cases, as that of Pepper (*Medical and Surgical Reporter*, 1883, xlviii, February

24, p. 197) it might be ascribed to hemorrhage, on account of its temporary character or sudden onset, in others it was due to the presence of leukæmic tissue in the ear. Politzer appears to have been the first to bring forward anatomical evidence of the latter (Otol. Congress, Basel, 1884, *Comptes-rendus*, p. 139). Later (*Arch. für Ohrenheilk.* xxiii. p. 242), Gradenigo reported a case of sudden deafness in leukæmia, partly disappearing. Post-mortem, there was evidence of chronic inflammation and old hemorrhages, with leukæmic growths in the mucous membrane of the tympanum. Gradenigo explained Politzer's case in the same way, believing the chronic inflammation a predisposing cause for leukæmic growths in the ear, and contrasted the tendency to hemorrhage in the eye in leukæmia with that of chronic inflammation of the ear in the same disease.

Exophthalmus was present in thirteen of the seventeen cases of chloroma. It was double in eleven. This, of course, depends on the involvement of the orbital periosteum and Tenon's capsule, which are affected not quite so frequently as the dura (and not always in continuity). The exophthalmus is, therefore, caused in the same purely mechanical way as in other tumors of the orbit, some of which, especially glio- and round-celled sarcoma, are not infrequently bilateral.

Exophthalmus has been described in leukæmia, and this is especially interesting from the fact that lymphoid tissue has never been seen or described in the orbit in health.

Leber (*Arch. f. Ophthalmologie*, 24. Jahrg., 1878, Abth. 1, p. 195) reported the case of a man of forty-eight years, with a leukæmia in which the red and white corpuscles were in almost equal numbers. Most of the leucocytes were small ones. There were large tumors on the eyelids, not adherent to the skin, going back into the orbit and not adherent to its margin. Both eyes were prominent. Under the conjunctiva tumors could be seen, having a dirty brown to violet color, as had those under the lids. There were swellings under the temporal muscles, which could not be distinguished from bone by the touch. There was hemorrhagic retinitis. The urine contained albumin and granular casts. The skin was pale; there was emaciation.

A bit of tissue removed from under the conjunctiva was soft, somewhat gelatinous. Microscopically, it showed closely aggregated mono-nuclear round cells in a delicate, wide-meshed, fibrillary connective tissue, not very well vascularized. The lymph glands in the neck were enlarged; the manubrium somewhat thickened and painful. There was great weakness, pain in the head, at times convergent squint, and thirst. The tumors in the temporal region became larger; the liver reached to the umbilicus; the spleen was enlarged. Exophthalmus increased, the swelling over the sternum reached the size of a fist, and tumors appeared in the parotid and submaxillary region. The patient died fourteen months after the tumors appeared in the orbit and six months after the leukæmia was recognized. No autopsy was made.

The resemblance of the case to most of those of chloroma is remarkable. Leber thought the tumors in the temporal region were from the bone-marrow, as I did in my own case, though every surgeon knows how deceptive the hardness of a tumor often is.

Leber quoted the case of Chauvel (*Gaz. hebd.*, 1877, No. 23) which was similar to his own in many respects, but in which the blood was not examined, though leukæmia was suspected.

Osterwald (*Arch. f. Ophthalmologie*, Bd. xxii., Abth. 3, p. 203) reported a case from Leber's clinic which is even more important in connection with chloroma than the preceding. The patient was a boy of four years. In April, 1881, a slight paralysis of the face appeared, and then receded. Then exophthalmus developed, flat swellings appeared in the temporal regions, the skin became cachectic, and there was loss of appetite. By May 25th there was double exophthalmus, dilated veins, and submucous hemorrhages; the tumors in the temporal region measured four to five by three to four centimetres in extent.

Leukæmia being suspected by Leber, the blood was examined and red and white corpuscles found in the proportion of 3–4 : 1. There was emaciation, and anæmia of skin and mucous membranes; on the skin a few petechiæ (flea-bites?). The skin bled easily; the blood was unusually thin and watery. No glands enlarged, except those behind the angles of the jaw. The liver extended two cm. beyond the costal margin; the spleen could not be felt. There was no pain or tenderness over the sternum. Later there was œdema of the eyelids; epistaxis; fever; pulse frequent, later slow, small, soft, and thready; tonic flexor contractions, tremors, and death, after repeated nose-bleed, three months after the beginning.

At the autopsy, flat, yellowish, "almost pus-colored," and tolerably firm neoplasms were found on the cranium, along the sutures. On the frontal were softer and reddish tumors. There were tumors in the walls of the transverse and cavernous sinuses and on the dura, of yellowish green, "durchaus eiterähnlichen" color, but hard. There were also areas of atrophy of bone, with osteophytes. At the base of the brain, and in the convolutions of the Sylvian fissure and optic thalamus, were hemorrhages.

There were ecchymoses all over the surface of the heart, under the pleura, and in the lung. The spleen weighed 71 grammes; it was soft, of pale brown color. The liver weighed 760 grammes. There were petechiæ in the stomach; the epigastric lymphatic glands were large, partly of greenish-yellow purulent appearance. There was also slight swelling of the mesenteric glands. The axillary glands were enlarged. On the ribs and along the vertebræ were leukæmic growths. The marrow of the ribs and right femur were of a brownish-green color and soft consistence. The diagnosis was myelogenic leukæmia, with leukæmic neoplasms as the cause of the peculiar symptoms.

Leucocytes occurred especially in two forms: most of them were of 1½ to 2½ times the diameter of a red corpuscle; the others the size of, or smaller than, red corpuscles.

The growths in various parts showed a leukæmic or lymph-adenoid character. Fibrous tissue varied in amount in different parts. (Osterwald reported the case especially as an example of the bacterial origin of leukæmia, for which see the original article.)

Birk (*St. Petersburger med. Wochenschr.*, 1833, viii, p. 377–86; *Fortschr. der Med.*, 1884, p. 138) has also reported a case beginning with intermittent fever, weakness, headache, swelling of liver and spleen. The lymph glands became enlarged; there was pain over the sternum. Examination of the blood showed a ratio of 1 : 3. The colorless cells were smaller than the red corpuscles, with few exceptions.

Exophthalmus came on suddenly, in both eyes, with loss of sight. Both testes became swollen; double pleural effusion came on, and after the appearance of œdema of the lower extremities the patient died. After death uniform infiltrations were found in various parts of the body. The exophthalmus was due to the formation of "new-formed lymph glands in the posterior part of the orbit."

Arnold and Becker (*Archiv. f. Ophthalmologie*, Bd. xvii.) and Bernheimer (*Bericht üb. die Heidelb. Ophthal. Gesellsch.*, 1889, p. 199; *Centralbl. f. allg. Path.*

u. path. Anat., 1890, p. 211) have reported cases of localized lymph-adenoma of the orbit. In a case reported by Kelsch and Vaillard (*Annales de l'Inst. Pasteur*, iv. 276) diagnosed *intra vitam* as leukæmia, but probably not entitled to that name, lymphoid tumors formed under the eyelids. It might be supposed that the lymphoid tissue could take its origin from the so-called "trachom" glands of the eyelid, but at least in the cases of so-called leukæmia with orbital tumors such an origin seems out of the question. (In regard to orbital lymphoid tissue, see Zaluskowski, *Arch. f. mik. Anat.*, Bd. xxx. p. 316.)

The case of Osterwald, even to the color of the new growths, is so like those of chloroma that it might seem proper to include it among the latter. For obvious reasons I have not done so. In the cases of Birk and Leber there is strong reason to suspect chloroma, but in the absence of more exact knowledge it is just as useful to keep them among leukæmic cases, showing, as they do, the peculiar localization of the chloromatous tumors.

In all cases in which the general condition of the patient is described, anæmia was marked. In a number of cases conditions closely related are described. So, in King's case there were petechiæ in the very beginning, and even at that time a slight blow caused severe hemorrhage; ten days later a blow on the face caused extensive extravasation as low down as the clavicle. By the end of the fourth week it was noted that health had failed. There were hemorrhages under the conjunctivæ, the skin (in a previously healthy "country-looking" girl) clear and bloodless.

In Aran's case there was early epistaxis, which was abundant every day for two weeks. There were anæmic murmurs over the heart and in the neck, and remarkable general anæmia. Aran spoke of the disposition to hemorrhage in his analysis of cases.

In the case of Durand-Fardel there was nose-bleed for eighteen months before admission. The skin was puffy and waxy and very anæmic.

In Mackenzie's case there was nose-bleed twice.

Balfour noted a bloody effusion under the conjunctiva.

Dittrich, whose case is reported chiefly from the post-mortem point of view, speaks of symptoms of "scorbutus." The body was pale, with few post-mortem discolorations; the blood like meat-water.

In Huber's case the patient was pale and anæmic; the cadaver pale, with few post-mortem discolorations.

In Chiari's case there was hemorrhage in the retina (but also new growths in the bulbs).

In Waldstein's case there was great anæmia early, and leukæmia appeared shortly before death.

In my own case all the blood symptoms noted, except characteristic scorbutic signs, were present.

In addition to Waldstein's case and my own, in which the proportion

of red and white corpuscles were those found in leukæmia, Huber noted in his own case, post-mortem, that in the blood, "in addition to the usual elements, among which the leucocytes were decidedly increased ('entschieden etwas vermehrt'), there were bodies which in all respects corresponded to the cells found in the new growths."

In regard to nose-bleed, it might be supposed the bleeding was due to pressure on the veins, but no other evidence of congestion was present. A similar explanation might be advanced for the retinal hemorrhage, but here again other evidence of obstruction is absent. In Leber's case of leukæmia, as in my own of chloroma, there was no choke-disk.

We have found, then, that in chloroma we have new growths which are like those of leukæmia, and which occur in the organs affected by those in leukæmia, either primarily or secondarily. We find, also, a complexus of symptoms which agrees, not only in its broad and striking features but also in detail, with that of the other condition. Three out of the nine cases examined since leukæmia was known show an increase of the leucocytes, two of them an increase such as is seen usually only in leukæmia. In the other cases no blood examinations were made, and we know that it is quite possible for a leukæmic blood to present no appearance that would attract attention. That makes the resemblance of chloroma to leukæmia greater, but there are two things that prevent us from going farther and claiming identity. These are, the short time in which increase of leucocytes has been observed in chloroma, and the unsatisfactory status of the term leukæmia.

Whether the increase of colorless corpuscles came on late, or was present during a longer period in my own case and in Huber's, can never be known. In Waldstein's case it was very late.

In rapidity of course, in general, chloroma stands between ordinary cases of leukæmia and those described by Ebstein (D. *Arch. f. klin. Med.*, Bd. lxiv. p. 343) as cases of acute leukæmia, one of which was Waldstein's case of chloroma. (The view advanced in the article just cited, that there is an essential difference between acute and chronic leukæmia, still requires confirmation.)

Chloroma also has a shorter course than is the rule in pseudo-leukæmia, but in the latter, too, we find exceptions.

Here, again, the possibility of a transition like that which is seen sometimes when leukæmia develops in the course of pseudo-leukæmia must be borne in mind, being exemplified in chloroma in the case of Waldstein's.

The greatest obstacle in attempting to show the possible relations of chloroma and leukæmia depend on the facts that we have so little knowledge of the anatomical basis and the clinical limitations of the latter.

Virchow's prophetic "Ich vindicire für die farblosen Blutkörperchen eine Stelle in der Pathologie" ("Weisses Blut und Milz Tumor," 1. Art.,

Med. Zeitung, 1846, Aug.-Sept., Nos. 34–36, and *Abhandlungen zur Wiss. Med.*, 2. ed., 173) has been followed by countless researches in the physiology and pathology of those bodies, and yet in the almost half-century that has elapsed how much more do we know than is contained in the following (*ibid.*, p. 192)?—"Leukæmia is not merely a purely anatomical, but essentially also a pathological conception. Not merely is the simple fact of the increase of the colorless corpuscles expressed, but, at the same time, the deficiency of red corpuscles, or, as I have emphasized from the beginning, the altered tissue formation of the blood in its dependence on certain organs."

We have, to be sure, learned much regarding the clinical features of leukæmia, and have widened its pathological anatomy, but our knowledge of its essential nature is not far from that expressed in the statement that it is "an albinism of the blood." (Virchow, *loc. cit.*)

Up to a very recent time the increase of the leucocytes was almost all that was needed to make the diagnosis. That is, the original idea of Virchow, that the difference between leukæmia and other conditions with increase of leucocytes—termed by him leucocytosis—depended on the permanence of the former (Virchow, *Path. Geschw.*, ii. p. 566, and *Cell. Path.*, Am. ed., p. 205: "Leukæmia is thus a sort of permanent progressive leucocytosis," etc.). But as more was learned of the transitory leucocytes, it was found that their differentiation, early or late, was not always easy. The attempt was then made to fix an arbitrary line between leucocytosis and leukæmia, and the idea of Magnus Huss, proposed long before (*Arch. gén. de Méd.*, 1857, ii. p. 308), to make the diagnosis when the proportion of white to red rose to 1 : 20 or more, was so eagerly taken up by clinicians that it seems to have answered a universal demand, which indeed it did—the demand for diagnostic signs. But like so many of them, it was found unavailable either to make a diagnosis or to confirm one when most needed. (Huss himself said the sign was to be used only when others—swelling of spleen and cachexia—were present.)

A new era opened when Ehrlich (*Zeitschr. für klin. Med.*, i., H. 3, p. 553, and *Farbenanalytische Untersuchungen zur Hist. u. Klinik des Blutes* Th. i. p. 51), announced that "an absolute increase of the eosinophile cells took place in leukæmia," or, as expressed in another place (Schwarze, *Inaug. Dissert.*, Berlin, 1880, and *Farben. Unters.*, p. 94): "The only pathological process in which the eosinophile cells are increased in mentionable manner is leukæmia. When one considers that the usual methods of examination frequently leave us in the lurch when the question between extreme leucocytosis or leukæmia arises, and when one considers that the beginning of this disease is almost beyond our diagnosis, the discovery (*Auffindung*) of eosinophile cells must be recognized as a grateful enrichment of our diagnostic methods."

The hope aroused by these statements, which were abundantly investigated, proved to be illusory, for many observers found an increase of eosinophile cells in various conditions quite different from those claimed by Ehrlich, and found them diminished (see below) in cases of leukæmia. But even before the observations alluded to were generally known, Erhlich, through his pupil Spilling (*Inaug. Dissert.*, Berlin, 1880, and *Farb. Unters.*, p. 71), admitted that the appearance of mononuclear cells with neutrophile granules was more distinctive than that of either the eosinophile cell or the "Mastzellen" (which Ehrlich had at one time looked on as important).

Still later (*Char. Annalen*, Bd. xii., and *Farb. Unters.*, p. 129), Ehrlich repeated this claim for the mononuclear neutrophile cells, though limiting their appearance to cases of myelogenic leukæmia ("Da nach meinen Erfahrungen die geschilderten mononucleären neutrophilen Zellen beim Erwachsenen unter keinen Umständen im Blut erscheinen, stellen sie das feinste und sicherste Reagent einer auf leukämischer Basis beruhenden Myelæmie dar, die auf diesem Wege schon in den ersten Anfängen mit Sicherheit erkannt und von jeder andersartigen Vermehrung der Weissen Blutkörperchen unterschieden werden kann.") At that time Ehrlich still claimed that the increased appearance of eosinophile cells was an additional sign of the same disease, "as the only place of formation of the cells in question is in the bone-marrow, "although he admitted, as before, their occurrence in normal blood.

Soon after this, Müller and Rieder ("Eosinophilen Zellen im circulirenden Blut,"*Arch. f. klin. Med.*, Bd. xlviii.), not only confirmed Ehrlich's claim regarding the mononuclear neutrophile cells, but went much farther. In the first place they identified Ehrlich's cell just named with the "Markzelle" of Müller, which the latter had in an earlier article shown to be the same as the myelocyte of Cornil, "cellule medullaire." (*Arch. f. klin. Med.*, Bd. xlviii., p. 47 *et seq.*)

While Ehrlich claimed his cell to be diagnostic of myelogenic leukæmia, Müller and Rieder held it to be so of leukæmia in general (*loc. cit.*, p. 119). "It is probable," they continued, "that the bone-marrow is always affected (a view which v. Ziemssen has also defended), although a slight change can easily be overlooked. We are therefore at present of the opinion that myelocytes will be found in all cases of leukæmia, even in the so-called lymphatic form."

In these two articles Müller and Rieder called attention to the important fact, previously overlooked, or not correctly estimated, that the eosinophile cells in leukæmia were remarkable more for appearing in unusual forms than in increased numbers.

They also gave the results of observations, confirming the earlier ones of Neumann (*Berl. klin. Wochenschr.*, 1878, No. 41, pp. 607 and 608), Cafavy (*Lancet*, 1880, ii. p. 769), and Löwit (*Sitzungsber. der kais. Akad.*

in Wien, 3. Abth., May, 1887), in regard to the diminished amœboid motion of the leucocytes on leukæmic blood in the warm stage, and suggested this as an additional diagnostic point.

Very soon after giving out the statements regarding the myelocytes, Müller had reason to modify them. In a case of lymphatic leukæmia, in which, by the way, eosinophile cells were present only in the proportion of one to several thousand, the myelocytes were so scarce that Müller was led to believe that "in many cases of lymphatic anæmia they could be entirely absent." (*Arch. f. klin. Med.*, Bd. l. p. 55.) The possibility was exemplified by a case observed by Rieder. This was a case of rapidly fatal lymphatic leukæmia, in which the proportion of white to red corpuscles rose to 1 : 12 (red 3,700,000). Most of the cells (about 90 per cent.) were lymphocytes. A very few normal eosinophile cells were found, but no myelocytes. There were, also, no nucleated red corpuscles. No myelocytes could be found in blood forming organs, nor were mitoses present. The bone-marrow presented lymph-adenoid hyperplasia (Neumann). (Rieder, *Beiträge zur Kenntniss der Leukocytose, etc.*, Leipzig, 1892, p. 38 *et seq.*)

It seems important to lay these facts briefly before the reader, on account of the confusion surrounding the subject and the necessity of indicating the difficulties attending the interpretation of the case under consideration. It seems important, too, because from the history of the eosinophile cell we may expect the myelocyte to be used, on the grounds of the early reports, long after its original advocates have changed their opinion as to its value. In fact, there is a distinct tendency even now to carry not only the diagnostic but also the pathognomonic value of this cell to an extreme not warranted by the facts. (I have not thought it advisable to mention in the body of the paper that the theory of Müller of the origin of the myelocyte is by no means universally accepted. Hayem, Löwit, and Troje (*Berlin. klin. Wochenschr.*, 1892, No. xii. p. 285), hold ideas opposed to those of Müller and differing among themselves. (The works of v. Limbeck, Rieder, and Hayem, and the articles cited above, can be referred to.) Recently Wertheim has brought forward, though very modestly it must be said, another cell claiming to be important in leukæmia—a spindle-shaped leucocyte. This must be even less distinctive than any other cell claimed to be specific (*Zeitschrift für Heilkunde*, 1891, pp. 308, 314).

From what has been said it might seem that the search for a specific cell in leukæmia has brought us back to our original position. But in the meantime we have learned some things that should make our disappointment thereat less keen. For this we have really to thank Ehrlich, whose painstaking and ingenious investigations have made possible all that has been gained, and who should, if for no other reason, not be held responsible for all that has been said in his name.

The advance alluded to is indicated in the following attempt to formulate a description of leukæmic blood:

It has a diminished number of red corpuscles, some of which have nuclei (normoblasts usually), though in some cases of lymphatic leukæmia there are no nucleated red corpuscles. The leucocytes are increased, usually to an extreme degree, and the increase is constant, though in some cases even great variations occur. The colorless corpuscles, in most cases, are characterized by the altered proportion of mono- and polynuclear forms, by the appearance of eosinophile cells in unusual numbers and of mononuclear neutrophile cells (Ehrlich, myelocytes, Markzellen of others). In some cases eosinophile cells and myelocytes are absent, or the former, if present, few in number (lymphatic leukæmia). *Most frequently and most characteristically, the cells vary more in size than those of the same classes in normal blood and in the so-called leucocytoses.* The leucocytes, especially the abnormal forms, show less active amœboid motion on the warm stage than usual. Less characteristic elements of leukæmic blood are poikilocytes, macro- and microcytes, "Mastzellen," karyokinetic figures in normal or abnormal cells, and Charcot's crystals (on standing).

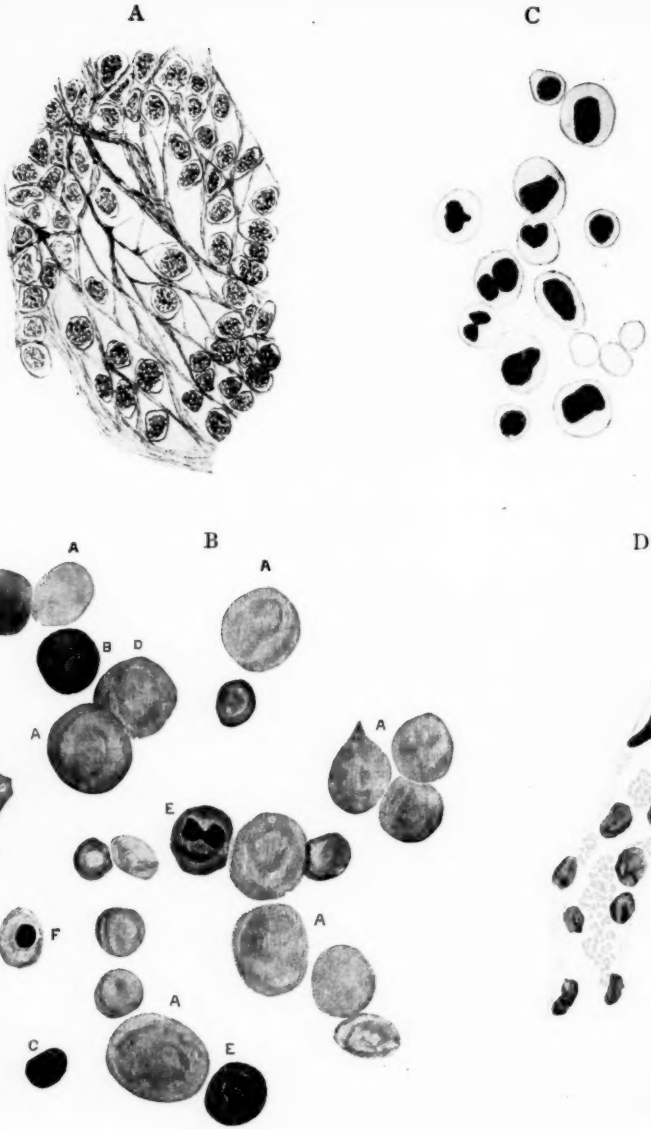
This statement, which agrees in the main with the conclusions of Rieder (*loc. cit.*, p. 36), is based on a careful analysis of the recent literature of leukæmia, and the examination of several cases of that disease.

The difference in size of the corpuscles seems important. In a case of lymphatic leukæmia, in which small lymphocytes formed almost all the leucocytes, the only eosinophile cells found—not more than one in many hundreds—were not more than half the average size found in healthy blood.

In two cases of splenic-myelogenic and three of myelo-splenic leukæmia the very small and very large polynuclear forms were very striking. These are found in the (human) marrow in non-leukæmic diseases, but not, I believe, in the blood. With our present means of investigation, we must give up the idea of finding a new and specific cell in leukæmic blood.

The distinction between leukæmias depending on disease of one or another blood-forming organ, or of combinations of organs, cannot be made from the blood alone, although very accurate guesses can be made in some cases, especially by taking the other conditions into consideration.

The attempt to separate the lymphatic form of leukæmia from the others cannot yet be said to have been successful. Notwithstanding the difference presented in some cases, not only by the blood, but also by the clinical symptoms (rapid course), on the other hand, in other cases the usual clinical picture is presented; and transition forms and combinations occur so often that the unity of the leukæmic process cannot yet



A. Pencilled section from the orbital tumor. Hardened in Mueller's fluid, stained with Bismarck brown; drawn from the camera lucida on Zeiss stand, tube in, 1/12 imm., oc 3, at level of stage

B. Blood from finger-tip, heated one hour at 120° C., stained with methylene blue and eosin. *a*, *b*, large lymphocytes; *c*, small lymphocytes; *d*, large mononuclear; *e*, polynuclear; *f*, normoblast. The leucocytes were drawn from the central part of one field; the normoblast introduced from another field; only a few of the red corpuscles were drawn. Zeiss, 1/12, oc. 4, tube in; drawing 17 mm. below the stage.

C. Blood corpuscles in pulmonary vein (lung section). Hardened in absolute alcohol, cut in paraffin, stained with hæmatoxylin and orange G. Same conditions for drawing as in B. All the leucocytes in one group, but only three red corpuscles, were drawn.

D. Renal tubule with greenish-yellow pigment. Hardened in alcohol, cut unimbedded, stained with alum-carmine. Amplification as in B.

To face page 179.]

be abandoned. The statement regarding the size of the leucocytes applies only to those fixed in a thin layer—all the cells flat. In a layer in which rouleaux have formed, wet or dry, the largest cells may not seem larger than red corpuscles.

From the above it would appear that we should be able to recognize leukæmia in the earliest stage; but so far, I believe, this has not been done. Practically, we can see how tedious the necessary examinations might be.

We do seem, however, to have reached a stage at which we can claim to have criteria for developed leukæmia, though even for this we must await the confirmation that only time can give.

With this necessary digression, we can return to the consideration of my own case of chloroma, and study the blood, the characteristics of which, I believe, are peculiar.

The most striking forms are the large lymphocytes, which occur in the proportion of 65 per cent. These are from the diameter of a red corpuscle to three times that width (see Plate: figure B, *a*). In hæmatoxylin (Delafield's), they take a pale greenish-blue color; in methylene blue a pale blue, and in Ehrlich's "triacid" appear as clear spaces with hardly any color. Only the smaller ones (see Plate: B, *b*) stain well, though not so deeply as the small lymphocytes. These cells show no distinction between nucleus and protoplasm. Some of them take the methylene blue more strongly in narrow areas around the edge—not complete rings. In the fresh blood, these cells do not seem nearly so large as when dried.

Small lymphocytes occur in the proportion of 7 per cent. These vary slightly in size, as shown by the figure (B, *c*), stain well in all nuclear stains, are homogeneous or coarsely granular, and show (with hæmatoxylin-eosin only) a very narrow rim of protoplasm.

Normal mononuclear and transition forms are present to the extent of 8 per cent. (1½ and 6½). They vary much in size. The nuclei of the transition forms usually stain well, those of the mononuclear less strongly. Mononuclear cells with neutrophile granulations cannot be distinctly made out. Out of a large number of covers stained with a mixture (Ehrlich's) that gave brilliant results with other specimens, Dr. Huber could find only three that were even suspicious. I thought I found two, but am very doubtful. They certainly were not typical.

Polynuclear cells form about twenty per cent. of the leucocytes. Their nuclei stain well, but the granulations are not as distinct as in normal blood. The cells of this class show the greatest variation in size. Those in the Plate (B, *e*), show the mean or normal; many are not more than half that diameter, a few are larger.

Normoblasts occur in proportion of two to five per thousand of red corpuscles (B, *f*).

Only one eosinophile cell has been found, out of many thousands of leucocytes. This was found by Dr. Huber, who with great patience carefully stained and examined a large number of imperfectly spread cover-glasses. I have recently gone over a large number of preparations without finding one more.

No mitoses can be found.

The proportion of white to red corpuscles, from a large number of fields counted is 24.74 : 100.

Certain points regarding the blood require special consideration.

The most numerous form of leucocyte is the large lymphocyte, the individuals of which vary considerably in size from those found in normal blood. They differ also from the latter in that, almost without exception, they show no protoplasms around the nucleus. This characteristic does not appear in the cells of the same class hardened in the bloodvessels. Figure C in the Plate was drawn with the same lenses and at the same level as B. It is easy to recognize in it the various kinds of leucocytes found in the fresh blood. In tissues hardened in various ways the results are the same so far as this feature is concerned. It seems rational to think that the peculiar conditions regarding the cells under consideration represent degenerative phenomena, although that does not advance our knowledge.

The small lymphocytes are increased, though not enough for us to say they exceed the normal limit. These cells differ so markedly in size and intensity of coloring from the large ones, that is easier to draw the line between them than in ordinary cases. Many of them look like free nuclei, especially the nuclei of normoblasts, but with hæmatoxylin and eosin a narrow rim of protoplasm may be made out. They never show the "grating" appearance.

The characteristics of the polynuclear and mononuclear cells have been sufficiently described. It is interesting to note the negative point, that the large cells of these classes having a faintly staining or clear protoplasm are very scarce.

The nucleated red corpuscles are all normoblasts. The large proportion of these cells is interesting in connection with other peculiarities of the case. In many respects this resembles lymphatic leukæmia. In the case of Rieder, mentioned before (*loc. cit.*, p. 40), no nucleated red corpuscles were found. Hayem (*Du Sang*, pp. 860, 864) has described a case of lymphatic leukæmia (red, 3,720,000; white, 476,-200) without nucleated red corpuscles. Müller, in the case alluded to, found them, though few. In his case there was lymphoid bone-marrow. Wertheim (*Zeitschrift f. Heilkunde*, 1891, Bd. xii., p. 314) in a case of lymphatic leukæmia found none. (In this case the blood-count was —red, 2,525,000; white, 480,000, *i. e.*, 5.2 : 1; hæmoglobin, 55 per cent.). Thayer (*Boston Med. and Surg. Journ.*, February 23, 1893, p. 184) says that in lymphatic leukæmia nucleated red corpuscles are rare, and when present are often megaloblasts. (See Neumann, *Arch. f. Heilk.*, 1872, xiii. p. 507.)

It has been supposed that nucleated red corpuscles only occur in cases of leukæmia in which the bone-marrow is involved, but this seems irrational (see opposing statements of v. Limbeck, *Grundriss einer klin. Path. des Blutes*, 1892, p. 161, and Bizzozero and Salvioli, *Centralbl. f. d. med. Wiss.*, 1879). That the appearance of these cells depends on an irritation of bone-marrow in the sense of Ehrlich ("Ueber schwere anæmische Zustände," *Verh. des XI. Cong. f. in. Med.*, 1892, Sep. Abdr.,

p. 13) can easily be granted, but as both Neumann and Müller found these bodies in the liver in large numbers it is by no means necessary to assume that.

The almost total absence of eosinophile cells is noteworthy, because it too is common in the lymphatic form of leukæmia, but even more so because the eosinophile cell appears to be a normal constituent of blood. I have examined in vain for a case in which they were as scanty as in this one and in a case of lymphatic leukæmia alluded to above. Guttmann (*Deutsche med. Wochenschr.*, 1891, No. 43, p. 1201) has mentioned a case of lymphatic leukæmia in which the spleen was also affected, in which only a single eosinophile cell could be found in a preparation. Wertheim (*loc. cit.*) found none. Müller in his case of lymphæmia (*loc. cit.*) found very few. Thayer (*loc. cit.*) in one case found only 0.1 per cent.

The absence of cells with basophile granulations in the blood, and their existence in the tissues in increased numbers, is interesting.

The absence of Charcot's crystals—the blood and pieces of liver and spleen were kept until putrid and examined daily with negative results—is another interesting feature in this case, especially in connection with the absence of other signs of disease of the bone-marrow.

The proportions of red and white corpuscles are worth emphasizing. Although it is true in many cases that in lymphatic leukæmia the increase of leucocytes is not so marked as in other forms, it is often considerable. In the cases of Müller, Wertheim, Hayem, and Guttmann already quoted, the proportions were 1 : 6, 1 : 5 2, 1 : 8, 1 : 1.4.

We find, then, in chloroma, blood which in its altered character coincides with that found in leukæmia. The conclusion is obvious, but before drawing it, it is necessary to consider another phase of leukæmia —that expressed in the words, "the altered tissue-formation of the blood in its dependence on certain organs."

It is often forgotten that we do not as yet know the origin of the leukæmic leucocytes, any more than of the normal ones. Efforts to explain the origin of leucocytes by facts observed in leukæmia, as might have been expected, have not made the subject any clearer, for observations have been interpreted in diametrically opposite ways.

The theory most widely accepted is that originated by Virchow and widened by Neumann, viz., that the leucocytes in leukæmia are derived from certain (hyperplastic) organs regarding which it is supposed, as the result of other observations, "that they stand in a certain relation to the formation of blood." These organs are the spleen and lymphatic glands and the thymus (Virchow, *Path. Geschw.*, ii. p. 566), and the bone-marrow (Neumann, *Centralbl. f. d. med. Wiss* , 1869, *Arch. f. Heilk.*, Bd. xi., *Berl. klin. Wochenschr.*, 1878, Nos. 6, 7, 9, 10).

The value of the evidence in favor of the splenic and lymphatic origin of leucocytes can be gathered from the fact that by many the bone-

marrow is looked on as the chief or only source of the excess of leucocytes in leukæmia.

This view or combination of views of the matter stands in direct contradiction to that of Kottmann (" Die Symptome der Leukæmie," *Inaug. Dissert.*, Berne, 1871), Biesiadecki (*Wien. med. Jahrb.*, 1876, p. 233), Löwit (*Sitzungsb. der k. Akad. in Wien*, 1885, Bd. xcii., Abth. 3), and others.

Notwithstanding the ingenuity and expertness with which Löwit defends his view, there can be little doubt that the view of Virchow-Neumann, at least in its broad outlines, will ultimately be shown to be correct.

But the latter view has been enlarged along with the increase of ideas of blood-formation, in the acceptance of the myelogenic form of leukæmia, and if we admit a participation of the organs mentioned, we must also admit the possible participation of the other known lymphoid tissues, the innumerable peripheral lymph nodules of the body. (See Flemming, *Arch. f. mik. Anat.*, Bd. xxiv.)

This brings up an interesting aspect of leukæmia, that relating to the so-called metastatic or heteroplastic growths, the history of which has been one of change.

Virchow originally (*Path. Geschw.* ii. p. 568), looked on these as heteroplastic neoplasms, so that " a sort of lymphatic tumor developed in organs in which normally no such formations occurred." The supposition that these were due to deposits of cells from the blood was rejected by Virchow, who held they originated *in loco*, as undoubted new formations.

But under the irresistible influence of the emigration doctrine Virchow's idea lost ground. This was hardly to be wondered at when men could go so far as, *e. g.*, Rindfleisch (*Lehrb. der path. Gewebelehre*, 1886, 6th ed., p. 211), who claimed a resemblance between leukæmic heteroplastic tumors and hemorrhages, though he held also that active emigration had some part in the process.

Bizzozero (*Arch. f. path. Anat.*, Bd. xcix. p. 378), however, revived the old teaching when he showed that active mitosis was going on in the secondary leukæmic tumors. His observations have been confirmed by Müller (*Arch. f. klin. Med.*, Nos. 48 and 50), and Wertheim (*loc. cit.*), and with the reaction now going on in regard to the extent of emigration in general, the true relation of the secondary leukæmic tumors is likely to be accurately determined.

Although it was believed very early (Virchow, Friedreich) that part of the leucocytes in leukæmia came from the secondary growths, but little importance has been attributed to those growths by later writers. Recently, indeed, if he is correctly reported, Virchow (*Berl. klin. Woch.*, 1892, No. 12, p. 289) has stated that the growths have no importance in the production of leucocytes, and that they are formed only in the

latter part of the disease. The question of early or late appearance seems to me to be a relative one, though it is true as a rule that the leukæmic lymphomata occur late in the disease.

But in regard to the possibility of some of the leucocytes being derived from the lymphomata, I think we must admit that the evidence is quite as strong as that regarding the origin of leucocytes from the spleen, thymus, bone-marrow, or peripheral lymph nodules.

Moreover, in many instances, it is difficult or impossible to say whether a given lymphomatous structure is hyperplastic or heteroplastic. In fact, when we consider the obscurity surrounding the development of the lymph nodules, when we remember that we do not know whether the lymph corpuscles are formed by division of similar ones in the nodules (Flemming), or are derived from the cells of the reticular tissue (Baumgarten), or the endothelium (Ribbert), and when we consider not only the possibility, but the strong probability of the origin of lymphocytes in the lymph spaces, we can see the need of a reconsideration of the secondary lymphomata.[1]

From what we do know of the natural history of leukæmia and of chloroma we can see the analogies of the diseases. We can say that chloroma is a lymphomatous process similar in its clinical features to leukæmia and pseudo-leukæmia. Our ignorance of its precise relations depends partly on the fact that our knowledge of chloroma is very incomplete, partly on the indefinite nature of leukæmia and pseudo-leukæmia. Whereas in leukæmia and pseudo-leukæmia there is for the most part a hyperplasia of the lymphoid tissue with which we are most familiar, in chloroma there is hyperplasia, perhaps heteroplasia of tissue closely related to the others, but even less understood.

In endeavoring to learn more of chloroma we find ourselves facing problems of the greatest interest, but problems that at present cannot be solved.

In my own case the insignificant enlargement of the lymph glands, thymus, and spleen (the latter two being involved only by localized neoplasms), seems incapable of accounting for the large numbers of leucocytes. It is impossible to say that the bone-marrow was not altered, since all the bones were not examined, but on account of the condition of the blood and from the results in other cases we can exclude such a complication with much confidence. We can hardly avoid the conclu-

[1] The point just alluded to must be worked out without reference to differences between the lymphocytes and other leucocytes in circulating blood. The recent investigations into the rôle of the fixed cells in inflammation, especially those of Ziegler and his pupils, the renewed interest in the connective tissue or lymph-space corpuscle, the "dormant" cells of Shakespeare (Medical News, Philadelphia, 1832, vol. xl. 1), and "Schlummer Zellen," of Grawitz (Arch. f. path. Anat., Bd. cxxvii., and Berl. klin Wochenschr., 1892), open up a promising field in all lymphomatous diseases.

sion, therefore, that the source of a large part of the leucocytes must have been the chloromatous growths. A careful examination of hundreds of sections of vessels of various kinds in the green tumors convinces me that no difference can be made out between the majority of the colorless corpuscles in the blood and lymph vessels and those in the adjacent lymphoid tissue.

If we assume that the cells have wandered out from the vessels we must suppose the excess of leucocytes was either produced in the vessels, or in blood-forming organs apparently little diseased. Moreover, the cells are such as least easily pass through vessel walls actively, and if forced through passively we should at least find many polynuclear cells in the tissue, which is not the case.

The absence of mitoses does not invalidate the supposition that the cells in the tumors have formed there (Bizzozero, *loc. cit.*).

To designate the cases as lympho-sarcoma adds nothing to our knowledge. Although it is no longer believed, as it was at the beginning, that in lympho-sarcoma there is never an increase of leucocytes in the blood, it is better in any case in which such an increase does occur to separate it from the category of sarcoma. Nor is it a gain to throw such cases in a distinct group along with those of lymphatic leukæmia, unless efforts to separate the lymphocytes from the other leucocytes genetically, are more successful in the future than they have been in the past, and even then the etiological factor might be a common one.

Looked at from every point of view, it seems better to class chloroma, for the present, along with leukæmia, pseudo-leukæmia, and myeloma, and to endeavor to work out its anatomical and clinical features on the same lines as those necessarily followed in the others.

Comparing chloroma with ordinary cases of leukæmia or pseudo-leukæmia, one cannot but be struck by the resemblance of the former to the process in those cases in which an insignificant epithelial tumor, primary in the uterus, gall-bladder, or intestines, produces early and enormous secondary growths in many organs.

Again, there is a striking resemblance to infectious (parasitic) processes. So long as we do not know whether leukæmia, as ordinarily met with, is due to vegetative excesses originating in the organism, or to irritants (parasites) from without, it is idle to speculate at length.

The clinical aspects of chloroma call up the possibilities of an infectious origin, which, of course, was suspected for leukæmia at the very beginning. In the case of Osterwald, which I strongly suspect to be one of chloroma, it was claimed that micro-organisms were found; but here, as in most of the cases of leukæmia and pseudo-leukæmia in which similar claims were made, the evidence is insufficient.

The symptoms of chloroma are so striking, and in many respects so uniform, that it is not only possible to make a diagnosis during life, but

in about half the cases it should be possible to do so at a very early period.

The important points in the diagnosis are: The appearance, usually below the age of twenty, of anæmia without evident cause, with loss of strength, dyspnœa and emaciation; hemorrhages in skin, mucous membranes (epistaxis), or internal organs (retina); rapid pulse; ocular symptoms, such as difficulty of vision, strabismus and especially exophthalmus, without the special features of Basedow's disease and with tumor in the orbit; deafness and ringing in the ears; and tumors under the temporals, or on the cranium in other parts, or in other parts of the body. Before the appearance of tumors the diagnosis would be doubtful, but after the appearance of tumors in the orbit and under the temporals, it could be made almost with certainty.

In such cases the blood should be examined by all the methods known, either to detect an increase or alteration of leucocytes already present, or, if that be not found, examinations should be made at short intervals in order to observe the possible advent of a leukæmic condition, which might come on only a short time before death.

The spleen, liver, lymph glands, and bones should be examined with reference to alteration in size and tenderness.

Although the essential points in the diagnosis were laid down by Huber, in no subsequent case was the disease thought of before death. It is to be hoped that, by calling attention once more to the subject, later cases may receive investigation directed to the elucidation of the many points yet unsettled.

THE ANATOMY OF THE VERMIFORM APPENDIX.

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I desire to call attention to some of the surgical relations which this now important portion of the intestinal tube makes with its surroundings—based upon the examination of 74 bodies in the dissecting-room of this college.

The points which presented themselves to my mind were:

1. The position of the vermiform appendix in relation to the ileum.
2. Its relation to the colon.
3. The relation of the colon to pelvic cavities.
4. The length of the appendix.
5. The distance from the anterior superior spine to the base of the vermiform appendix.

6. The distance from the umbilicus to the base of the vermiform appendix.

7. Amount of mesentery:

(*a*) at juncture of vermiform appendix with colon;

(*b*) and its extent on vermiform appendix.

8. Distance from umbilicus to anterior superior spine.

9. Inter-iliac measurement.

To these might be added the distance from the anterior superior spine to the apex of the vermiform appendix, and the distance from the umbilicus to the apex of the vermiform appendix; but not having made a sufficient number of measurements on these points, I hesitate about placing any importance upon them. They are here appended, however, in the hope that others may be stimulated to add to them.

Of the 74 subjects examined, 56 were white males, 10 white females, 6 colored males, and 2 colored females.

Twenty-one subjects of the 74 gave evidences of pathological lesions about the appendix, divided as follows: 16 white males, 2 white females (one of whom had been operated upon), and 3 colored males.

The position of the vermiform appendix in relation to the ileum should be discussed, as—

a. Below the ileum, extending into the true pelvis.

b. Below and behind the ileum, extending into the true pelvis.

c. Below the ileum and remaining in the ventre of the ilium.

d. Below and behind the ileum, remaining in the iliac ventre.

e. Below the ileum and above the innominate crest.

f. Behind the ileum and above the innominate crest.

Of the 56 white males, 2 were below the ileum and extending into the true pelvis; 12 were below and behind the ileum, extending into the true pelvis; 12 were below the ileum and remaining in iliac ventre; 22 were below and behind the ileum, remaining in the iliac ventre; 7 were below the ileum and extended above the innominate crest, and 1 was behind the ileum and extended above the innominate crest.

Of the 10 white females, 2 were below the ileum, extending into the true pelvis; 2 were below and behind the ileum, extending into the true pelvis; 4 were below the ileum, remaining in the iliac ventre; and 1 was below and behind the ileum, remaining in the iliac ventre; and finally, in 1 the whole specimen had been removed after operation.

Of the 6 colored males examined, 2 were below and behind the ileum and extending into the pelvis; 1 was below the ileum and remaining in the iliac ventre; and 3 were below and behind the ileum, remaining in the iliac ventre.

Of the 2 colored females examined, 2 were below and behind the ileum, extending into the pelvis.

It will be observed that in 28 subjects—taking both races and sexes

together—the most frequent position for the vermiform appendix in relation to the ileum was below and behind, remaining in the false pelvis. The next most frequent was below the ileum, remaining in the false pelvis. In sixteen subjects the vermiform appendix was either below and behind the ileum, in the cavity of the true pelvis, and the remaining eight were either below or behind the ileum and above the innominate crest, *i. e.*, not in the false pelvis even.

The variations in the position, as is known, are accounted for by the development of the peritoneum, which allows or prevents the descent of the caput coli into the pelvis.

The position of the vermiform appendix in relation to the colon should be discussed as it starts on its inner, inner and posterior, posterior and inferior aspects.

Of the 56 white males examined, it occurred six times on the inner; forty-four times on the inner and posterior; four times on the posterior; and twice on the inferior aspects.

Of the 10 white females examined, it occurred six times on the inner and posterior; twice on the inner; and once on the posterior aspects; and one post-mortem removed.

Of the 6 colored males examined, it occurred five times on the inner and posterior, and once on the inner aspect.

Of the 2 colored females examined, it occurred in both instances on the inner and posterior aspects.

It will be observed that in 57 subjects the position of the vermiform appendix was on the inner and posterior aspects of the colon, and in the order and number of frequency—inner, eight; posterior, six; and inferior, two.

The position of the colon in relation to the pelvic cavities should be considered in four different ways, viz.: In the ventre of the ilium. In the ventre of the ilium, extending into the true pelvis. Above the ventre, and in contact with abdominal viscera.

The colon was observed in 56 white males, in the ventre of the ilium, forty-four times; in the ventre, extending into the true pelvis, eight; above the iliac ventre, three; and in contact with lower surface of the right lobe of the liver and on top of the right kidney, once.

In the 10 white females it was found in the iliac ventre, seven times; and in the iliac ventre, extending into the pelvic cavity, twice; and one post-mortem removed.

In the 6 colored males the colon was in the iliac ventre, three times; in the iliac ventre, extending into the true pelvis, twice; and in contact with the liver, once.

In the 2 colored females it was observed in the iliac ventre, twice.

There are, therefore, 56 subjects in which the colon occupied the ventre of the ilium; 12 in which it extended into the true pelvis from

the iliac ventre; and 2 in which it was attached to abdominal viscera. All these variations in the viscera depending upon peritoneal support, depend upon two facts: the amount and rapidity of development of the peritoneum and the varieties of food taken by the individual early in life while the intestinal tube is most sensitive.

The length of the vermiform appendix was measured—

In white males, 56 times: maximum 17 cm.; minimum 2.5 cm.; average, 9.09 cm.

White females, 9 times: maximum, 9 cm.; minimum, 2.5 cm.; average, 6.7 cm.

Colored males, 6 times: maximum, 16 cm.; minimum, 7 cm.; average, 11.2 cm.

Colored females, 2 times: maximum, 11.5 cm.; minimum, 7 cm.; average, 9.2 cm.

Of the total number, 73 subjects, the average length was 8.97 cm.

The distance from the anterior superior spine of the ilium to the base of the vermiform appendix was observed—

In white males (55): maximum, 16 cm.; minimum, 3 cm.; average, 7.5 cm.

In white females (10): maximum, 10 cm.; minimum, 4 cm.; average, 7 cm.

Colored males (6): maximum, 10 cm.; minimum, 5 cm.; average, 7 cm.

Colored females (2): maximum, 7.5 cm.; minimum, 6 cm.; average, 6.7 cm.

The average measurement for all classes, distance from anterior superior spine to base of vermiform appendix, 7.2 cm.

The distance from the anterior superior spine of the ilium to the apex of the vermiform appendix was only taken twenty times. White males (15): maximum, 20 cm.; minimum, 1 cm.; average, 8.5 cm. White females (3): maximum, 11 cm.; minimum, 3 cm.; average, 7.3 cm. Colored males (2): maximum, 11 cm.; minimum, 7 cm.; average, 9 cm. The average measurement for all classes, from the anterior superior spine of ilium to apex of vermiform appendix, 8.3 cm.

The distance from the umbilicus to the base of the vermiform appendix was observed in 46 white males, with a maximum of 15 cm.; minimum, 4 cm., and average, 7.8 cm. In 8 white females, with a maximum, 14 cm.; minimum, 5 cm.; average, 9.1 cm. In 5 colored males, with a maximum, 13 cm.; minimum, 8 cm.; average, 10 cm. In 2 colored females, average, 11 cm. The average distance from the umbilicus to the base of the vermiform appendix, 8.1 cm.

The distance from the umbilicus to the apex of the vermiform appendix was observed in 8 white males, with a maximum, 20 cm.; minimum,

3 cm.; average, 10.1 cm. In 3 white females: maximum, 15 cm.; minimum, 8 cm.; average, 11 cm. In 2 colored males: average, 9 cm. The average distance from the umbilicus to the apex of the vermiform appendix for all classes, 10.1 cm.

The amount of mesentery measured at the juncture or commencement of the vermiform appendix and the colon was taken in 55 white males, the maximum being 10.5 cm.; minimum, 5 mm.; average, 2.85 cm. In 4 white females: maximum, 4 cm.; minimum, 2 cm.; average, 3.1 cm. In 4 colored males: maximum, 3.5 cm.; minimum, 5 mm.; average, 2.1 cm. In all classes, mesentery at the beginning of vermiform appendix, 2.78 cm.

The amount of mesentery on the vermiform appendix and its extent thereon from the base to the apex was measured in 37 white males, with a maximum length of 10.5 cm., a minimum of 5 cm., and an average of 4.7 cm. Other measurements were taken in two instances in each of the other classes, but do not give any data to work upon. The average, however, is 5 cm.; *i. e.*, this is an average amount of mesentery that may be found, supposing that the length of the appendix is 8.91 cm.: or, about one-half its length.

In sixteen white males the mesentery extended the whole length, also in seven white females, in one colored male, and in one colored female. In two subjects it was so bound down that no measurement could be taken at all, and in one subject there was no mesentery whatever.

This great variation in the amount of mesentery belonging to the appendix would lead me to this conclusion, namely, that one must always expect to find a mesentery extending more than half the length of the appendix, and that from its free extremity one must expect great latitude of position—which may be assumed both on account of its length and also on account of the manner in which its mesentery is attached.

The distance from the umbilicus to the anterior superior spine of the ilium was taken in white males forty-nine times, with a maximum of 18 cm. and a minimum of 10 cm., the average being 12.4 cm. In white females, eight times, with a maximum, 15 cm., and a minimum, 12 cm.; the average being 13.7 cm. In colored males four times, with a maximum, 15 cm.; minimum, 12 cm.; average, 13.7 cm. In colored females twice, maximum, 19 cm; minimum, 15 cm.; average, 17.2 cm. The average for all classes, 12.8 cm.

It goes without saying that in multiparæ this measurement should be considerably changed, but that in the male the change in adult life would not occur until adipose tissue became decidedly developed.

The inter-iliac measurement, from one anterior superior spine to the other, was taken in 50 white males, with a maximum of 30 cm. and a

minimum of 19 cm., the average being 22.4 cm. In white females seven times, with maximum, 25 cm.; minimum, 22 cm.; average, 23.3 cm. In colored males six times, with maximum, 25 cm.; minimum, 21 cm.; average, 23 cm. In colored females twice, maximum, 21 cm.; minimum, 20 cm.; average, 20.7 cm. The average for all classes, 22.5 cm.

It was, of course, impossible to obtain very accurate histories of the bodies examined, consequently it is impossible to verify certain points which, from these investigations, would naturally arise. I have therefore confined myself to visible topographical points.

1508 PINE STREET

MASSAGE IN MUSCULAR RHEUMATISM, AND ITS POSSIBLE VALUE IN THE DIAGNOSIS OF MUSCULAR RHEUMATISM FROM NEURITIS.

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THE muscles of the lumbar region and their fascia are a favorite seat for muscular rheumatism, which is then called lumbago, as everyone knows. This may arise from catching cold, from strain, from fatigue, or from rheumatism in the system. The pathology of this affection is probably coagulation of the semi-fluid contractile muscular substance and adhesion of muscular fibrils, so that attempts at motion are accompanied with partial, irregular, and painful contractions. Retention of waste products occurs, and it is pretty generally conceded that uric acid is the worst of these, thus adding "fuel to the fire" and pressure upon nerve filaments. Recent cases of muscular rheumatism are sufficiently common to anyone engaged in the practice of massage. They are almost invariably cured by a few massages, sometimes by a single massage. The same result may be brought about by rest, by warmth, by electricity, or by the administration of medicines that eliminate uric acid, such as salicylate of soda, though I think not so soon. Any of these may be used separately, combined, or with massage, thus affording us a choice of one hundred and twenty combinations of these five measures ($1 \times 2 \times 3 \times 4 \times 5 = 120$). But which of these is the most effective single agent could only be determined by the skeptical if they could have lumbago or muscular rheumatism sufficiently often to try each one separately, and massage last of all; for in therapeutics this is a science of experience, and not one of experiment, as it would be in physiology when tried on healthy persons. A wearisome detail of cases

of recent muscular rheumatism successfully treated by massage is unnecessary. It is the object of this article to show that in these, massage produces changes in five different ways: mechanical, thermal, electrical, nervous, and chemical. The *mechanical* change is shown by muscular rigidity being replaced by suppleness and elasticity, minute adhesions having doubtless been detached and the coagulation of the muscular substance replaced by the semi-fluid condition. The matting together of skin, superficial fascia, and deep fascia is also removed by appropriate massage, so that the skin glides more freely over the tissues beneath it. The pressure of the previous turf-like condition is taken away from the vessels and nerves so that patients feel lighter and more supple and freer from restraint. The *thermal* change is evident from the increase of heat, imparted from the hand of the manipulator as well as that arising from the massage and from the accelerated circulation. The *electrical*, also an objective change for which we do not need to take the patient's word, is manifest by more vigorous and agreeable contraction of the muscles to the faradic current after massage than before. For the *nervous* change we have to take the patient's word for improved sensation in the disappearance of pain, discomfort, and the feeling of stiffness. The *chemical* is inferred from the removal of waste products and uric acid, by the increased circulation and flow of lymph, which in plain language removes the ashes, flushes the *sewers*, and takes away asphyxiated juices, while the increased arterial current brings a greater supply of nourishment; otherwise improvement would hardly take place. The constipation of the tissues is got rid of, let the refuse matter be what it may.

Dr. Haig has shown pretty conclusively[1] that when chilling of the surface checks the excretion from the skin, diminution of the alkalinity of the blood and retention of uric acid take place in the tissues beneath. The same result follows when fibrous tissues have been injured, strained, or excessively fatigued: uric acid accumulates in the affected parts, superadding its irritating properties, and this may be abstracted from the blood to such an extent as to show an increased alkalinity of the urine owing to diminished excretion of uric acid. This condition can be got rid of by salicylate of soda, or by alkalies. When recent, it can also be more promptly dispelled by means of massage, thus showing that this has brought about chemical changes. If massage and alkalies, or salicylate of soda, be used simultaneously, the medicine will act more quickly by reason of the improved circulation resulting from massage—as most, if not all, medicines do when the case is such as to admit of massage. This is a fact too often unrecognized, and frequently redounds unduly to the credit of massage; as when a

[1] In the London Practitioner for March, 1891.

patient has for a long time been taking a remedy that is clearly indicated, but shows no improvement until massage has been used. On this subject let us hear from old Fuller, in his *Medicina Gymnastica*, published in 1771: "It is to be considered that some medicines may require exercise (of the patient) in order to enhance their virtues or to remove some inconvenience attending their operation which might deter people from using them so freely as they ought to do. The ordinary circulation of the blood may not suffice to answer the nature of some medicaments and call out their efficacy. Exercise in such cases is like the just and exact incubation to the egg—that which animates the drug and gives it power to produce the desired effect."

It is hardly necessary to state here that whatever treatment be adopted for acute muscular rheumatism, the diet should be regulated, and highly nitrogenous foods and acid wines interdicted for a time.

Zabludowski, Hopadze, and others have found by careful observation that general massage on healthy people increased the excretion of urates and phosphates, and the assimilation and metamorphosis of nitrogenous food substances.

As to the mechanical effect of massage, we might learn a lesson from nature. Adhesions of the pleura are often detached by the rubbing together of the two membranes in respiration. The fascia of muscles is a sort of pumping arrangement by which lymph is sucked out of the muscles and propelled onward into the lymphatics. It consists of two layers, between which are lymph spaces terminating in lymphatic vessels. When the muscles contract, the inner layer is pressed against the outer and forces the fluid onward into the lymphatic vessels. When the muscles relax, the inner layer recedes from the outer and the lymph from the muscles finds its way into it and the lymph spaces between. Hence by the contraction of muscles, waste products are washed out of them by the flow of fresh lymph. But patients with a severe attack of lumbago cannot exercise. In such cases, massage is more than a substitute for exercise, so much more, indeed, as the pressure of massage may be greater than the pressure which muscles make upon each other during contraction. In my *Treatise on Massage*, I have not only described the manner of using massage in such cases, but also the effects of friction and deep manipulation in the direction of the lymph and venous currents. The veins and lymphatics are mechanically emptied, the blood and lymph are pushed along more quickly by the *vis a tergo* of massage, and these fluids cannot return by reason of the valvular folds in the internal coats of these vessels. More space is thus created for the returning currents coming from beyond the region *masséed*, and the suction power induced at the same time adds another accelerating force to the more distal circulation. In brief, the effects

may well be likened to the combined influence of a suction and force pump, and in people that are not too fat the veins can be seen collapsing as they are emptied and filling up again as their contents are pushed along by the hands of the manipulator. In this way the collateral circulation in the deeper vessels is aided and relieved, as well as the more distal stream in the lymphatics, capillaries, and arterioles. One would naturally suppose that the circulation in the larger arteries would in this manner be interrupted, and such is the case. But herein comes an additional advantage to aid the circulation, for the temporary and momentary intermittent compression causes dilatation of the arteries above the parts pressed upon, from an increased volume of blood, and as soon as the pressure is removed this accumulation rushes onward with greater force and rapidity into the partially emptied continuation of the arteries, in consequence of the resiliency of the arteries and the force of the heart's action upon the accumulated volume of blood.

The difference in the consistency of muscles is of much interest. The muscles of some very strong people are soft and flabby when relaxed; of others, hard and firm. This difference is no indication of muscular power or the want of it. It is due to the condition of the fascia that surrounds the muscles. When this is thick it gives a feeling of hardness; when thin, of softness. The contractile substance of muscle is semi-fluid, as has been shown by Kühne. The same difference exists in dogs and other animals. The muscles of short-haired dogs are usually hard and firm; of long-haired ones, soft and flabby; and Ludwig has shown that the former yield much lymph, the latter little. Lauder Brunton is of the opinion that this difference in the deep fascia may account for the tendency to muscular as distinguished from articular rheumatism. Where muscles are soft from thin fascia, the tendency to muscular rheumatism is probably greater; whereas persons whose muscles feel hard from thick fascia most likely have a tendency to articular rheumatism. When the fascia is soft and thin the products of waste from over-exertion or other causes would incline to remain and occasion muscular pain; when the fascia is hard and thick, waste products would be removed more quickly from the muscles and might give rise to inflammation of the joints.

I think there must be much truth in Dr. Brunton's opinion, for I have seen cases of muscular rheumatism where the muscles felt preternaturally firm and hard, so much so that one might imagine that a quantity of plaster-of-Paris had been injected under the skin and allowed to set, which under massage became soft and supple as they improved. The following case, though a somewhat obstinate one, is an example of this:

CASE I.—Mr. J., a large, stout gentleman, had been subject to attacks of rheumatism in the trapezius, deltoid, or lumbar muscles all his life. At one time he was seized suddenly and severely with pain in the lumbar region, so that he could not even attempt to move. I was called to him the first day of this attack, and found all the muscles of his back, but especially those of the lumbar region, rigid, hard, and board-like, and almost insensitive to pressure. Perhaps the lessened sensation to external impression was owing to the already existing severe pain. Issues of vast importance depended upon his recovery in a short time, so massage was given twice daily for a week. At the end of this time the muscles were supple and elastic, sensitive, even tender to pressure; but the pain had disappeared and the patient could move freely.

Treatment is sometimes used to prove the diagnosis, as when iodide of potassium is given in cases of doubtful syphilis. Reasoning in the same way, Dr. Haig asserts that when any local irritation is not increased and made worse by acids given to the extent of distinctly raising the acidity of the urine and diminishing the alkalinity of the blood, or is not improved by alkalies given to the extent of decided diminution in the acidity of the urine or increase in the alkalinity of the blood, or by a salicylate given to the extent of producing a great increase in the excretion of uric acid, then such local irritation is not directly due to uric acid.

In the same manner I would venture the suggestion that when a case of apparent muscular rheumatism does not only yield but also does not stay improved after a few massages, then the probability is that the case is one of neuritis affecting the nerve fibres that supply the impaired muscles. This probability would be strengthened when the pain is uniform, affecting the same muscles on both sides, when it is worse at night whilst the patient is at rest and warm in bed, and better when up, moving about, which calls into play the inhibitory action of the will; whereas muscular rheumatism is aggravated by motion and relieved by rest and warmth. The difference in favor of neuritis would be increased when the consistency of the affected muscles does not differ from that of the well muscles or is somewhat diminished. Of course, it is not a question here of marked cases of neuritis where the pain is confined to one or more nerves and their distributions, with atrophy of muscles, altered electrical reactions, glossy skin, etc.

The relief from discomfort, and freedom of motion experienced after each massage in those cases which are too apt to be snappily diagnosed as muscular rheumatism, but most likely are neuritis, is so great that, though the temporary improvement may not be held, yet the patient is apt to demand that the massage be continued until the ultimate result, which, with appropriate internal medication, should be recovery. The following cases may be cited as examples:

CASE II.—Mr. D. was sixty-three years of age, and had always enjoyed good health, with the exception of frequent attacks of asthma. He was well nourished, having a due proportion of muscle and adipose. He came to me in July, 1887, suffering with stiffness and discomfort of the shoulders and hips, of several weeks' duration. This first showed itself in the hips. By reason of this discomfort he was restless and uneasy at night. At first sight the trouble seemed to be entirely muscular, and this view was strengthened by the result of treatment, for he had massage and passive motion early every afternoon nine times in succession, and after each massage he could bend over freely and rise from a chair without the assistance of his arms, cross each leg over the other with ease, tie his shoes, and dress himself, even to putting on his coat, as if there were nothing the matter with his shoulders, all of which he could not do before massage. This improvement continued the remainder of the day, but, unfortunately, next morning he was almost as stiff as ever. Though his deltoids and glutei did not appear to be altered in consistency, yet, after massage, they were much suppler and afforded corresponding freedom of motion. Evidently this patient ought to have had massage twice a day, so that the effect of one *séance* would not have been gone before he had another; but instead of this there was an interval of ten days in which he had none and grew rapidly worse. Then he had massage every other day three times, with but slight temporary improvement after each time. After this he tried travelling three weeks, during which he was drowsy and depressed, and came back worse than when he went away, so that it was with great difficulty that he could raise either foot high enough to get into a carriage—indeed, he had to ask his coachman to help him raise the leg for this purpose, and it was hard work for him to get into his coat even with assistance. He stooped like an old man. Pains in the fingers had also set in, so that it was difficult for him to hold a book. The muscles of the shoulders and upper arms, of the hips and thighs, had become somewhat atrophied and flabby, with diminished reaction to both galvanic and faradic currents, and increased irritability to percussion. Pressure on the large nerve trunks and muscles showed no tenderness. He was about four months getting into this, his worst condition, in which he remained for three months, and he was five months, or the balance of a year, getting well. During this time, as if by way of compensation, his asthma scarcely troubled him. He continued to get about and attend to business even at his worst. He had electricity occasionally in the daytime, and massage almost every evening on retiring, which gave him much relief and comfort and aided him to sleep better. He is firmly of the opinion that massage aided his recovery and shortened his suffering by at least one year.

This case was undoubtedly one of neuritis, and what is of the greatest interest is the fact that just before his first symptoms appeared he had been taking five drops of Fowler's solution of arsenic three times daily for six weeks for his asthma. Five months later arsenic was found in the urine in large quantities by Prof. E. S. Wood. During his recovery, the patient, on his own responsibility, took a secret preparation containing arsenic and hydriodic acid for his asthma. The neuritis that was most likely left by the arsenic in the first instance was probably benefited by the arsenic in

the secret preparation, and so thought an eminent neurologist, under whose care he was for a while.

CASE III.—Another case, very similar to the foregoing, came to me in September, 1891. It was that of Mr. C., sixty-seven years of age, weighing 168 pounds, who, though of pale complexion, had red lips, and had enjoyed remarkably good health all his life. Ten or twelve years before, he had slight lumbago. For about four weeks pain and stiffness in the shoulders and hips, at the back of the neck, and between the shoulders, had been gradually increasing, so that it was not easy for him to put on his coat or button his shoes. He was worse at night after he had been in bed some time, and also in the morning, but improved somewhat after getting up and moving about. Every patient is a standard for himself as to the consistency of his tissues, and, so far as could be judged through this patient's adipose, the muscles seemed to be somewhat doughy and flabby, especially the deltoids and glutei. Those of the upper arms and thighs were apparently slightly atrophied and deficient in contractility to the faradic current. His appetite was not very good, and he had not taken a vacation for many years. Salicylate of soda had been thoroughly tried without any result. The immediate effect of massage from the first was magical, affording comfort and freedom of motion the remainder of the day on which it was given, which again led us to think the trouble altogether muscular. But his nights were still bad, and in the morning he was as stiff as ever. The longer he slept the stiffer he became. He continued the massage faithfully for eleven weeks, daily or every other day, always with great temporary relief, but, on the whole, gradually becoming stiffer and more uncomfortable. Iodide of potash, tonics, and the faradic current were in turn faithfully tried with the massage, but did not afford any more relief than massage alone. Ten grains of phenacetine in the evening and ten more when he wakes at night will give him a good night and a comfortable day after. But he has to omit this for a day or two before it will have this effect again. Five or six weeks after I first saw him, pain, stiffness, and thickening gradually came in the fore and middle fingers of the right hand, and the pain was also distinctly traceable in the course of the radial nerve.

I referred this patient to Dr. E. G. Cutler for further internal treatment, and under iron and cod-liver oil his general condition has improved and his appetite is better. For a month he has done nothing for his joints and muscles, and they remain in about the same condition. He requires assistance to dress. Like the preceding case, this gentleman attends to business at his worst. His own opinion is that if he could have massage on retiring its advantages to him would be much increased; but he lives out of the city. Unlike the preceding case, he is, so far, of a cheerful disposition. He has not been exposed in any way to arsenical poisoning; he has not taken any in medicinal form, and his wall-papers are free. He, therefore, regards it as superfluous to have his urine examined for arsenic, so it has not been done; neither has it for lead. He is a temperate man, so that alcohol does not enter into the case. Three weeks after he had been under massage the urine was examined by Dr. Cutler and found to contain a large normal amount of urea (12.25 grains to the ounce), due probably to increased tissue metabolism produced by massage. A large primary deposit of oxalate of lime crystals was also found. In other respects the urine was normal.

It is a pity that we are not absolutely certain that there is no arsenic in this patient's urine; for, if there be none, as most likely there is not, it would count strongly in favor of the arsenic found in the urine of the preceding case having nothing to do with producing his neuritis. As arsenic seemed to benefit the neuritis in the first case after the poison had been eliminated, then it might be a good remedy to employ for the second case. How much better arsenic may act while a patient is undergoing massage can only be conjectured. How much more quickly it may be eliminated while the patient is having massage is also a subject for consideration. Dr. G. Tedeschi[1] has reported a case of lead poisoning cured by massage after the usual treatment had failed. By this means he found that the urine was increased in quantity and the lead eliminnated more promptly than by any other means.

Case IV.—What is called rheumatism frequently affects both muscles and nerves. An acute case of rheumatic sciatica, intractable to the usual orthodox remedies, can sometimes be speedily changed for the better by means of massage, even when this does not afford such marked temporary relief as in such cases of neuritis as those just mentioned. In March, 1888, I was kindly asked by Dr. J. B. Ayer to visit his patient, Rev. B. H., fifty-eight years of age, who was well nourished, with tissues supple and elastic, except in the affected regions. He was then in his third attack of sciatica, or, more properly, rheumatic neuritis of the sciatic nerve, all three attacks having been traceable to his getting run down from overwork, and each attack having been preceded by lumbago, which faded away as the sciatica became more pronounced. The lumbago had affected the muscles on both sides; the sciatica, the right hip, thigh, and leg. The first attack had occurred eighteen years before and lasted for three months; the second came eight years after, and lasted for six months—worse than the preceding. The third attack had lasted severely for four weeks before I saw him, and, according to the same geometrical progression, we calculated and feared that he was in for a year of it, as anti-rheumatics, tonics, sedatives, galvanism and faradism had produced no sensible amelioration. We were agreebly disappointed, for, in four weeks and a half, under massage once a day, most of this time, with morphine when the pain became intolerable, he was, to all intents and purposes, well. Afterward, whenever he felt any premonitions of a returning attack, he had recourse to massage, a few applications of which has always afforded the desired relief. And this brings me to say that, when a patient has been benefited by massage, if a relapse or reappearance of the same trouble takes place, it is much more speedily relieved or cured by massage than it was at first; in other words, the patient has become more susceptible to its influence.

At the fifth visit massage was given to leg, thigh, and hip only, as the pain in the lumbar region had disappeared and suppleness of tissues had returned. The manner of using massage was by gentle stroking or *effleurage* on the posterior aspect of the limb, and deep, vigorous manipulation on the lateral and anterior aspects. Sometimes it is well to use deep pressure, so as

[1] Giornale interno delle Sci. Med.

to squeeze congestion out of a nerve, and then vigorous percussion over it, so as produce an obtunding effect; but these were out of the question at first in this case. The sixth massage seemed to rouse a slumbering soreness, and make the whole limb uncomfortable for an hour; but after this it felt better than before, and continued so. Subsequent massages after this had a similar effect. The reason of this was, without doubt, due to the detaching of adhesions which caused matting of the tissues. This required arduous work; but as suppleness and elasticity returned, the work became easier. At the twelfth visit, after forty minutes of massage to leg, thigh, and back, the patient felt that if I did any more it would certainly arouse the pain which the massage had just quieted. This was near the end of the third week, and he could run up and down stairs freely. And so the patient improved with interesting variations, pain decreasing and intervals of comfort increasing. On the thirty-first day after massage was begun he preached twice, superintended his Sunday-school (distributing presents to the children), and felt no worse for it. Sixteen massages in four weeks and a half, then a week's vacation, and he was himself again. But the external aspect of the leg, from the knee to the toes, has remained numb ever since.

Dr. A. Symons Eccles, in an article on "Massage, Rest, and Position in the Treatment of Sciatica,"[1] has reported several cases of sciatic neuritis in previously healthy people, which he treated successfully in this manner after the failure of other means. The massage consisted of *effleurage*, kneading, and percussion, and, in the intervals, the leg was suspended in a Salter swing, as this was the only position that afforded rest.

REPORT OF A CASE OF GANGRENOUS STOMATITIS, WITH A BACTERIOLOGICAL EXAMINATION.

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The case reported in this paper entered the New Haven Hospital October 26, 1892, and was in the service of Dr. W. H. Carmalt, through whose courtesy I was permitted to make a bacteriological examination.

The patient, Katie M., seven years of age, was born in New Haven, of Irish parentage. There was no history of tuberculosis or any other hereditary disease in the family. The patient had lost no brothers or sisters, and her father, mother, and four brothers and sisters were living and well. Though she had been brought up in a tenement-house the hygienic surroundings had not been particularly bad. When two years old she had a fall, striking her face on a piece of board and driving a small sliver of wood into the left malar region. The wound

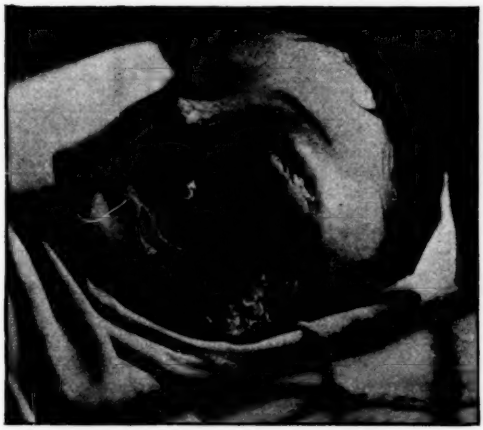
[1] London Practitioner, November, 1887.

suppurated and remained open for two months, but finally healed. Early in the summer of 1892 she had the whooping-cough. About the middle of September, 1892, she was taken sick with typhoid fever and was confined to her bed constantly from that time.

The present illness—*i. e.*, stomatitis—dates from the middle of October, 1892, when, the parents say, the patient had what they thought was an ulcerated tooth on the left lower jaw. The ulceration began in the gum, increased with great rapidity, and soon involved the inner part of the left cheek.

The patient was seen by Dr. T. H. Russell several days before her entrance into the hospital, who describes her condition somewhat as follows: Her left cheek had a round black necrotic patch about the size of a silver dollar, surrounded by a red, swollen, almost erysipelatous inflammatory area. The parents of the patient stated that the disease had

FIG. 1.



been apparently painless, and that the child was constantly picking at her teeth with her fingers, and finally pushed a finger through the necrotic patch on the cheek. After this the disease extended more rapidly, removing all the skin and muscular tissue of the left cheek and exposing the bone of the inferior and superior maxilla. The teeth on the exposed bones were loosened and fell out. The odor was extremely fetid. The appearance of the patient on entrance to the hospital can be better understood from the photograph than described.

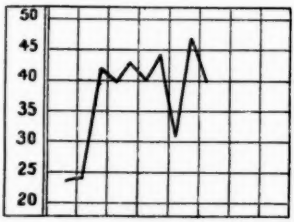
The remaining portion of the clinical history was mostly obtained from the hospital records.

On entrance, pulse 130, temperature 102.8°, respiration 25. Urine, specific gravity 1017; acid; no albumin; a considerable sediment of urates.

Oct. 30. The soft parts on the left side of the nose are almost completely gone to the median line. The cavity is bounded below by the lower border of the inferior maxilla, and above by the edge of the orbit. A large necrotic mass the size of a hen's egg was removed to-day. The tongue does not seem affected. Bowels and bladder act involuntarily. Patient lies in a kind of a stupor and does not seem in great pain.

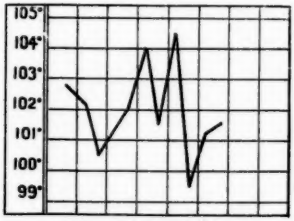
No record was made of the condition of the heart and lungs, though during the latter part of the disease the patient coughed considerably. Up to within two days of death she took nourishment well, taking over one quart of milk daily, and in addition wine whey and sherry wine. Occasional doses of Majendie's solution were given hypodermatically for relieving restlessness.

FIG. 2.



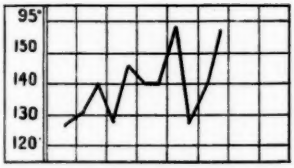
Respiratory chart.

FIG. 3.



Temperature chart.

FIG. 4.



Pulse curve.

The local treatment consisted in washing with Condy's fluid, and, in the application of charcoal poultices. Later, pure carbolic acid was painted about the necrotic area, but neither treatment had any effect in arresting the progress of the disease.

The patient died on November 1, 1892, about two weeks from the date of onset of the disease.

The causes of gangrenous stomatitis are predisposing and exciting. In infectious diseases the predisposing causes prepare the soil and the exciting causes furnish the infection.

The predisposing cause of gangrenous stomatitis is a weakened state of the body resulting from such diseases as measles and typhoid fever, combined with unhygienic surroundings. The exciting causes are local, and are not so plain. A necrosis is usually attributed to a disordered nutri-

tion, either from the cutting off of a blood supply by pressure, as in bed-sores, or by embolism or thrombosis; or from the cutting off of trophic nerve influence, as in ulceration of the cornea in animals when the fifth nerve is cut. None of these causes, however, either pressure, embolism, thrombosis, or neuritis, apparently are present in gangrenous stomatitis, and one is driven therefore to the conclusion that the local exciting cause producing the necrosis is the existence of some organism in the tissue which, either by its direct action or by the poisons it produces, causes a necrosis of tissue. But gangrenous stomatitis is not only a necrosis, but a gangrene—that is, there is not only death of the tissue, but putrefaction, and putrefaction requires the presence of bacteria of putrefaction, therefore it must be remembered that the bacteria producing the putrefaction are not necessarily the ones producing the necrosis. In fact, if we may trust the experiments of Lingard, the bacillus which he found in cases of gangrenous stomatitis produced a necrosis of the heart muscle in rabbits, but not a gangrene. It is quite possible that the putrefactive portion of the process in gangrenous stomatitis is produced by other bacteria. The cause of the necrotic process is, however, the most important, as necrosis is the primary change.

Our knowledge of the bacteriology of gangrenous stomatitis is based on the investigation of six cases—one by Schimmelbusch, and five by Lingard.

Schimmelbusch[1] found small bacilli, often in pairs, and sometimes in long filaments growing along the boundary line of the living tissue. These bacilli grew on gelatin without liquefying it, at the temperature of the room. They did not stain by Gram's method. When injected into rabbits, they produced local abscesses only.

Schimmelbusch did not prove that his bacillus had any etiological relation to the pathological process, but only made this hypothesis probable by finding the bacillus along the border of the healthy tissue.

Lingard also found a bacillus 4–8 micromillimetres long, probably the same as the one detected by Schimmelbusch, located along the border of the healthy tissue.[2] He found this bacillus constantly present in five cases, and cultivated it outside the body, though he does not state upon what media. When inoculated into the ear of rabbits it caused great swelling and redness, and death on the tenth day.

Examination of the viscera showed characteristic changes in the pericardium, which was covered with a false membrane in which bacilli were found. There were also patches of necrosis in the ventricular wall, containing bacilli. These changes are not found in the human heart. It is possible that the differences in the results of experiments on animals

[1] Manual of Bacteriology, Sternberg, p. 466.
[2] Lancet, 1888, ii. p. 159.

obtained by Schimmelbusch and Lingard may have been because the point of inoculation was different.

The examination of the case of gangrenous stomatitis which I have reported was begun on Oct. 27th, about four days before the death of the patient. It consisted in making smear cover-glass preparations, cultures, and animal experiments; of a microscopical examination of a portion of the healthy tissue bordering on the slough, which was removed after death; and of an examination of the blood.

I. *Cover-glass preparations.* After drying and flaming some were stained with carbol-fuchsin, some by Gram's method, some with Koch's alkaline methyl-blue, and some were treated with glacial acetic acid and a subsequent gentian-violet stain. In all the specimens there were vast numbers of staphylococci, streptococci, and diplococci, and a very few long bacilli, often in groups, stained faintly by Gram's method, but more deeply by other methods.

II. *Blood.* A special examination of the fresh blood was made to detect the motile crystal-shaped bodies described by Sansom, but none were found.

A blood-count showed about 1,600,000 red corpuscles to the cubic millimetre. The number of white corpuscles was 36,363 to the cubic millimetre, or about in the proportion of one white corpuscle to forty-four red ones. The amount of hæmoglobin was about 40 per cent. of normal. The white blood-cells were mostly polynuclear leucocytes, with a few mononuclear. Specimens stained with methyl-blue showed no bacteria.

III. *Cultures.* A small loop of sterilized platinum wire was pushed as deeply as possible into the sloughing tissue, twisted around, drawn out and rubbed successively over six or eight slant tubes of agar. Cultures were thus made on agar, glycerin-agar, and Weichselbaum's agar. In two or three of the last tubes inoculated the colonies were so few and well distributed that it was easy to make pure cultures as well as to distinguish different kinds of bacteria. Tubes of agar were also inoculated from the blood of the finger, but they remained sterile. All the cultures were kept at a temperature of 33°–35° C. Many colonies developed, from which pure cultures were made. These all proved to be micro cocci, staphylococci, streptococci, and diplococci, but no colonies containing bacilli were discovered, even after repeated examination. The colonies most abundant proved, by growing in gelatin, to be the staphylococcus pyogenes aureus, the streptococcus pyogenes, and the micrococcus cereus albus.

My failure to detect bacilli may have been due to the fact that the platinum loop was not pushed into the border of the sound tissue, where the bacilli are by far the most numerous, but into the centre of the slough.

The cultures were fortunately made before any vigorous antiseptic treatment had been adopted.

The day before the death of the patient an attempt was made to make some fresh cultures, but no colonies developed in the agar tubes which had been inoculated. This was probably because a small portion of the

carbolic acid saturating the slough was carried over by the platinum loop into the agar tubes.

IV. *Animal experiments.* Two rabbits (No. 1 and No. 2) on October 28th were inoculated through a subcutaneous incision in the abdominal wall, well beneath the abdominal fascia, with a piece of slough from the face of the child.

Oct. 30. The rabbits seemed stupid and did not eat much. There was an area around the point of inoculation about one inch square, much reddened and swollen in each rabbit.

Nov. 5. Both the rabbits seemed much better, but the swollen, inflamed areas mentioned above were evidently the seat of abscesses. Pus could be pressed out of them. Cover-glass preparations were made from this pus, and cultures also. The cover-glasses after staining showed abundant micrococci and staphylococci, and a very few single long bacilli. Abundant colonies of the micrococcus cereus albus developed on the agar plates, and also another large egg-shaped micrococcus which in gelatin-tube cultures presented a rapid white superficial growth without liquefaction. No colonies containing bacilli were found.

15*th.* Both rabbits are alive and well. Small nodules at the point of inoculation about the size of a pea. All signs of acute inflammation have disappeared.

Rabbit. No. 1 killed. The nodule mentioned proved to be a cheesy mass encapsulated in a wall of tough connective tissue. There was no peritonitis nor sign of former peritonitis. The heart appeared normal both macroscopically and microscopically. Nothing worthy of note was discovered in any of the viscera.

A new rabbit (No. 3) was inoculated in the ear with some of the cheesy matter in the nodule removed from rabbit No. 1. This resulted only in a slight inflammatory reaction with no swelling and very slight redness lasting only a day or two.

The encapsulated cheesy mass which was removed from rabbit No. 1 was hardened and sections made. Sections were stained by Kühne's method. A few masses of micrococci in the connective-tissue cells were found near the border of the cheesy area. No bacilli were found.

V. *Sections made from the skin covering the malar bone of child.* A slough of skin covering the malar bone at the border of the necrotic area was removed after the death of the child. (No autopsy was permitted.) This was hardened in alcohol and imbedded in celloidin. Sections were made and stained by Gram's method, with carbol-fuchsin, and by Kühne's method. The last method showed up well the pathological process as well as the bacteria growing in the tissue. The sections, as a rule, presented three areas—an outer one of necrotic tissue, a middle one of infiltration with round cells, and an inner one of normal tissue. The bacilli were most abundant and stained most deeply along the border of the necrotic area. In the interior of the necrotic area they did not take the stain so readily. The single bacilli measured $2\frac{1}{2}$ micromillimetres to $3\frac{1}{4}$ micromillimetres in length, but were often joined end-to-end in long strings. These bacilli were, in many places, the only bacteria seen, and were packed closely together to the exclusion of all other bacteria along the line of necrosis. This gave one the impression that they were eating

directly into the sound tissue. In the necrotic area, especially near the outer part, were seen micrococci and streptococci.

The bacilli were not entirely confined to the necrotic area, but could be seen infiltrating the sound connective tissue, though in much less abundance than along the line of necrosis. The bacilli were stained especially well by Gram's method. In using this method, however, great care needs to be taken not to decolorize too much.

My conclusions differ from those of Schimmelbusch in that the bacilli found by him did not stain by Gram's method, and from those of Lingard in that his bacilli were somewhat longer than those which I found. These differences in staining peculiarities and size may possibly be ascribed to differences of technique which further investigations may harmonize.

The finding of a bacillus characteristic in appearance, staining with Gram's method, far outnumbering all other kinds, and growing in innumerable numbers along the border of the necrotic area, in one case, certainly does not prove that it is the cause of the disease. It does, however, confirm one of the conclusions of Schimmelbusch and Lingard, and in view of the scanty literature on the subject seems worth recording.

REVIEWS.

DISEASES OF THE EYE. A PRACTICAL TREATISE FOR STUDENTS OF OPHTHALMOLOGY. By GEORGE A. BERRY, M.B., F.R.C.S. Ed., Ophthalmic Surgeon, Edinburgh Royal Infirmary; Senior Surgeon, Edinburgh Eye Dispensary; Lecturer on Ophthalmology, Royal College of Surgeons, Edinburgh. Second Edition, revised and enlarged. With colored illustrations from original drawings. Pp. xxii., 727. Philadelphia: Lea Brothers & Co., 1893.

THE first edition of this work appeared in 1889, and now in only four years we have the pleasure of perusing the second edition.

We must at the outset say that this is by far the best work upon its theme in the English language that we have seen, for the diction is pure and clear, and besides, the beautiful illustrations of normal and diseased conditions make it a valuable addition to the library of all practitioners, general as well as special. We have never seen more real delineation of disease, the coloring is perfect, and each illustration is an "object lesson."

Another great feature is, that the illustrations are to be found in the natural course of the text, and one does not have to stop and refer to some plate at the back of the volume.

There are one hundred and ninety-seven illustrations, of which ninety-three are colored, being drawings from nature, made by Dr. Tatham Thompson, of Cardiff, and Mr. Sydney Stephenson.

The volume is divided into eighteen chapters, a general index, and an index of authors. Chapter I., "Examination of the Eye," is clearly and distinctly treated of in forty-seven pages, and we are pleased to note the practical way in which the author has grouped the facts; especially well stated are the ophthalmoscopic appearances of the optic nerve in health, and the many curious vascular changes of the nerve head, shown in six drawings. Under the changes in the fundus in the aged, we note the lack of transparency in the optic nerve, and its muddy or dull look without any pathological change; also a condition of depigmentation of the retina, which may occur in patches, admitting of the structure of the choroid coming into view: both of these conditions we have seen, but they are rarely mentioned by writers. In speaking of ophthalmoscopes, he says: "Many forms of this instrument are in use, differing mainly in the form of mirror and the arrangement for bringing the different lenses behind the aperture. But there is a tendency to multiply the number of lenses and introduce refinements in the mechanism of hanging the mirror, etc., which only add to the cost, without in the least increasing the practical usefulness of the particular ophthalmoscope."

In speaking of the "light streak" on the retinal arteries, the author accepts Dimmer's theory that it is due to reflection from the blood corpuscles of the axial current of blood.

Chapter II., "Diseases of the Eyelids and Lachrymal Apparatus" occupies thirty pages, and is most perfectly illustrated in color; especially good are the two plates showing the course and direction of the lachrymal duct. We can fully concur in the remarks on the treatment of lachrymal diseases, especially that in reference to large probes, where the author says: "I am convinced that they either do no good or are postively hurtful."

In speaking of the causes of "nictitatio" and "blepharospasm," we fail to note any mention of errors of refraction as a cause; we have frequently noticed such, and immediate relief when proper correction followed.

Chapter III., "Diseases of the Conjunctiva." In this chapter the usual mode of treatment is carried out that we are all so familiar with, and it is to be commended. We would take exception to the remarks on the use of jequirity, where he says: "It is certainly unjustifiable to use it in cases where there is not very great defect of vision on account of pannus, ... as it is impossible to control the severity of the inflammation to which it gives rise." We believe, if the author had personal experience with this method of treating granular conjunctivitis, he would not so express himself, as we in this country find it of great service, and can fully control the resulting inflammation.

We notice also the failure to mention the method of treatment known as "grattage," which for the past few years has held full sway in certain quarters, although it is a method that will not stand the test of time.

"Electric-light Ophthalmia" is mentioned, and we only notice it to say that we wish authors would cease using the word "ophthalmia," unless they mean to express the idea that the whole tissue of the eye is involved in a general inflammation.

The article on "Keratitis" is particularly interesting; especially are we interested in the "dendriform" variety, of which a beautiful plate is shown.

Chapter V., "Diseases of the Crystalline Lens." Most interesting are the etiological facts narrated under this heading. Yet after all we come back to the old idea—summed up by the author thus: "It seems not unlikely that cataract in man is due either to circulatory disturbances in the nutrient fluid of the lens, or, though less frequently, to alterations in the chemical constitution of the nutrient fluid." In speaking of the operation of extraction of cataract, the author describes and is in favor of the method *with iridectomy*, and in speaking of the claims of those who prefer *no iridectomy*, for the reason of the resulting round pupil, says, "the game is, in fact, not worth the candle," with which we quite heartily agree.

The chapter on "Diseases of the Iris and Ciliary Body" is complete and richly illustrated, and the therapeutics up to the advanced methods employed in all our large ophthalmic hospitals.

Foreign bodies in the eye are treated in a very simple and conservative manner. If we had more of this kind of surgery promulgated we would have fewer sightless eyes.

When speaking of "Sympathetic Ophthalmitis," many things are said which go to show the author a close clinical observer and a safe leader; *e. g.*, "A soft eye, in which perforation, either from accident or ulceration, has at any time taken place, and which is tender to pressure, is that which endangers the safety of the other." Again: "A perforation which has arisen from within is not so liable to be followed by sympathetic ophthalmitis as one which has taken place from without."

After a full discussion of the pathology of this affection, he concludes by accepting the theory of the migration of germs through the lymph spaces from one eye to the other, as affording the most satisfactory solution of the problem.

Tobacco amblyopia is believed in by the writer; but we have yet to see or hear of the first case well authenticated: it must be that our English brethren use the "weed" more than we.

Section I. closes with an interesting chapter on "Hemianopia."

Section II. includes within one hundred and fifty pages "Errors of Refraction and Accommodation," and "Affections of the Oculo-motor Muscles." All the refractive conditions are treated in a simple and plain way, and also in smaller type are elaborated the formulæ and equations necessary to prove the result for those who wish to know the exact method by means of which conclusions are reached. This is of service, and meets the wants of the busy reader as well as the special student.

Javal's ophthalmometer (old model) is figured, and a description of the instrument given. The author says of it: "Though affording a simple and trustworthy means of calculating the amount of astigmatism, it has the disadvantage of being expensive." While this is partly so, yet the confidence felt by the examiner more than offsets the cost of the instrument.

An exhaustive chapter on "Convergent Strabismus," giving the different views advanced by various observers, concludes with the author's accepting the explanation of Hansen Grut, which makes squinting a mere phenomenon of *innervation*, and not due to any muscular defect, further stating that such explanation is but an extension to its natural conclusion of Donders' view.

Section III., "Operations," occupies the last sixty pages of the volume.

Antiseptic surgery is commended in its practical and common-sense way, but it is not believed in as a "fad." Thus: "Some few operators in Berlin attach importance to operating in an aseptic or supposed aseptic atmosphere. . . . . Such precautions are simply an evidence of an inability to understand the true nature of the sources from which the risks of septic inoculation arise."

In speaking of the operations for advancement, Prince's operation is preferred with slight modifications.

In concluding this too hasty review, we cannot but reiterate what we said at the beginning, that we have had great pleasure in the perusal of this work, and great profit, and that we consider it the best on the subject in the English language to-day, not only for its diction, but for its instructive illustrations. The publishers have given excellent paper and type. W. O. M.

RECENT CONTRIBUTIONS TO MEDICAL LITERATURE.

1. THE RETROSPECT OF MEDICINE: A HALF-YEARLY JOURNAL CONTAINING A RETROSPECTIVE VIEW OF EVERY DISCOVERY AND PRACTICAL IMPROVEMENT IN THE MEDICAL SCIENCES. Edited by JAMES BRAITHWAITE, M.D. Lond., Obstetric Physician to the Leeds General Infirmary, etc. Vol. CV., January–June, 1892; small 8vo., pp. xxi., 436. Vol. CVI., July–December, 1892; pp. xxii., 449. London: Simpkin, Marshall, Hamilton, Kent & Co., Limited.

2. THE DISINFECTION OF SCARLET FEVER AND OTHER INFECTIOUS DISEASES BY ANTISEPTIC INUNCTION. By J. BRENDON CURGENVEN, M.R.C.S., L.S.A., formerly House Surgeon of the Royal Free Hospital, etc. Read at meeting of the International Congress of Hygiene and Demography, held in London, August 14, 1891. 8vo., pp. 25. London: H. K. Lewis.

3. ON CONGENITAL OBLITERATION OF THE BILE-DUCTS. By JOHN THOMSON, M.D., Fellow of the Royal College of Physicians of Edinburgh; Lecturer on Diseases of Children, School of Medicine, etc. 8vo., pp. ii., 52. Edinburgh: Oliver & Boyd, 1892.

4. EPIDEMIC INFLUENZA: A STUDY IN COMPARATIVE STATISTICS. By F. A. DIXEY, M.A., M.D., Fellow of Wadham College. With diagrams and tables. 8vo., pp. xv., 29. Oxford: Clarendon Press, 1892.

5. DISEASES OF THE LUNGS, HEART, AND KIDNEYS. (No. 14 in the Physician's and Student's Ready-reference Series.) By N. S. DAVIS, JR., A.M., M.D., Professor of Principles and Practice of Medicine, Chicago Medical College, etc. Small 8vo., pp. vii., 359. Philadelphia and London: The F. A. Davis Co., 1892.

1. THE volumes of the *Retrospect* for the year 1892 present the profession with yet another proof of the merits which, for many years, have caused it to be a book of reference for the best medical literature of the day in a condensed form.

Naturally with so many articles by different authors, the degree of merit must vary greatly, but the articles that are not good are conspicuously few.

The present volumes, like those that have gone before, can confidently be turned to to furnish information of the latest advances in the medical sciences.

2. THE method of disinfection advocated by the author consists in smearing lightly the entire body of the patient night and morning with one of the essential oils, the best of which he holds to be the oil of eucalyptus. Better results are obtained, however, by combining two or three essential oils of different densities, since the air will then take up more of the combined vapor than when only one is used.

In the case of scarlet fever the inunctions are continued night and morning for three days. After the third day the skin is anointed only at night, after a warm bath, for seven days, when this treatment ceases and the patient joins the rest of the family.

In addition to the disinfection accomplished by this procedure, it is claimed that children become less restless and sleepless after inunction, and that the temperature drops several degrees, with a consequent lessening of the associated febrile phenomena. This latter result, however, can be obtained with any fatty or oily substance, as it is a well-known fact that free inunction of the surface with any fat, such as lard, for instance, will bring about a fall in temperature when pyrexia exists.

3. As the author rightly states in the preface to this monograph, there has never before been published a complete *résumé* of the recorded cases of this lesion. In the present work he has collected and classified forty-nine cases of this rare condition. By a series of tables, in which the clinical details and post-mortem appearances of these cases are clearly set forth, the value of the work is greatly enhanced. Indeed, the author may well feel satisfied that in this article he has presented the profession with a valuable addition to the literature of congenital malformations.

4. Considering the vast amount of literature that has been written upon the subject of epidemic influenza during the past few years, it is no small accomplishment to have composed an article that will undoubtedly assume a permanent place in the history of this malady.

The amount of labor which the author has expended in compiling the various tables of mortality, and other statistics, must have been enormous. Great as it seems to have been, however, it has been justified by the results attained. Unless we are greatly mistaken, the book will always stand as one of valuable reference for future investigators of this disease.

5. The scope of a work of this kind is naturally restricted to the bare statement of essential facts concerning the various diseases with which it deals. Designed as a book of ready reference, the author has accomplished his purpose; it is one more added to the already numerous members of this class of medical literature. Nevertheless, the book will prove a useful possession to the hurried practitioner and student, especially as a reference for treatment, to which the author has given particular attention.

The work deserves success. T. G. A.

An Introduction to the Study of Diseases of the Skin. By P. H. Pye Smith, M.D., F.R.S., Fellow of the Royal College of Physicians, and Physician to Guy's Hospital, London. Small 8vo., pp. 408. Philadelphia: Lea Brothers & Co., 1893.

This handbook is, in the main, a reflex of the author's own observations in the domain of dermatological medicine, and as this experience has been a large one, the book will be found to contain much of practical value to the student and practitioner. The subject matter is given in a clear, readable, and terse style. A special feature is the introduction of diagrammatic woodcuts for illustrating the local distribution of certain diseases. The introductory chapter deals with special etio-

logical and pathological factors, and a short and instructive chapter is added at the end of the book on practical classification and diagnosis. An appendix containing formulæ, description of the common soaps, the various baths and mineral springs, is also given.

The publishers have well contributed their part toward giving the volume successful presentation. H. W. S.

HANDBOOK OF MATERIA MEDICA, PHARMACY, AND THERAPEUTICS. By SAMUEL O. L. POTTER, A.M., M.D., M.R.C.P. Lond., Professor of the Theory and Practice of Medicine in the Cooper Medical College of San Francisco; Visiting Physician to St. Luke's Hospital, etc. Fourth edition, revised. Pp. xvi., 781. Philadelphia: P. Blakiston, Son & Co., 1893.

SCARCELY more than a year has passed since the reviewer carefully read the third edition of this book. The opinion of its merits which he then expressed has been verified by the favor with which it has been received by the profession. The present edition bears evidence of careful revision without presenting any departure from the original plan of the work. The sum total of the additions is fourteen pages, and yet this small addition by no means conveys a just idea of the improvements to be found. The newer remedies, as aristol, chloralamid, diuretin, phenacetine, and piperazine, are for the first time considered, and brief notices of phenolid, exalgine, salipyrine, and hypnal are found. We believe that this list could, with profit, have included salophen, hydrastinin, bismuth salicylate, and thiol. Many sections have been considerably enlarged, as those upon acetanilide, the treatment of alcoholism, of influenza, and upon drug eruptions. The appearance of the pages has been greatly improved, and study facilitated, by the more liberal use of display type. Very few typographical errors are found, in addition to those to which the author calls attention at the beginning of the book ("tincture of the chlorate of iron," p. 225). In the section devoted to patent medicines we find an increased number of formulas and a few changes in title. On page 741 the author presents a very valuable table for computing the dosage of active ingredients in each drachm of mixture, the total quantity of the ingredients and the amount of the mixture being known. The index has been increased to the extent of one-half of a page. The use of the former edition during the past year for study and reference has confirmed the opinion expressed in the review of that edition. "The author has very skilfully steered his course between the pessimism that marks a system of therapeutics based solely on the results given by experiments and observations in the chemical and physiological laboratories, and the optimism of hasty empirical generalizations upon meagre clinical data."

R. W. W.

PROGRESS

OF

MEDICAL SCIENCE.

THERAPEUTICS.

UNDER THE CHARGE OF

REYNOLD W. WILCOX, M.A., M.D., LL.D.,

PROFESSOR OF CLINICAL MEDICINE AND THERAPEUTICS AT THE NEW YORK POST-GRADUATE MEDICAL SCHOOL AND HOSPITAL; ASSISTANT VISITING PHYSICIAN TO BELLEVUE HOSPITAL.

The Treatment of Dysentery by Ipecacuanha *sine Emetinâ*.

Dr. A. Crombie has treated seven cases of catarrhal dysentery with this drug. He directs rest in bed, a milk diet (preferably peptonized), and opium generally in the form of Dover's powder, combined with bismuth and soda bicarbonate, twice daily. No observations were made upon the severer kinds of dysentery, the so-called "diphtheritic" and amœbic forms. This remedy caused vomiting in a considerable proportion of instances; but the vomiting, when it did occur, was not so distressing as that caused by ordinary ipecac; and was not a bar to its administration; no laudanum was given to mitigate its effect, nor to detain its passage through the bowels. Its administration was followed by improvement and recovery in six out of the seven cases in which it was given. Neither form of ipecac shows, however, any special advantage in the treatment of dysentery as compared with that by means of bismuth and Dover's powder, which causes no distress whatever. If, however, driven to use ipecac, the preference should be given to ipecac *sine emetinâ*.—*Indian Medical Gazette*, 1893, No. 4, p. 106.

Massive Alkaline Medication.

Dr. Henri Huchard shows that the alkalinization by the administration of massive doses of bicarbonate of soda is without danger. The "alkaline cachexia" is not to be feared; many clinicians have not hesitated to administer bicarbonate of soda in doses of from two and one-half to seven and one-half drachms. A case is cited of a man seventy years of age, who for ten years received each day a dose of from five to six drachms of bicarbonate of soda dissolved in a bottle of water, and that for combating a dyspepsia caused by an excess of hydrochloric acid. For the past four years he has

ceased to take this remedy, and his alimentary tract is completely restored to health. It is an error to believe that an excessive amount of this alkali is capable of producing an atrophy of the glands of the mucous membrane of the stomach; it is rather the excess of hydrochloric acid that is responsible for this condition. This use of bicarbonate of soda is of great value in dyspepsia characterized by the production of an excess of hydrochloric acid, and even the amount mentioned above may be materially surpassed. In diabetes, either in the form of lime-water, or as bicarbonate of soda, or as tartrate of soda, this treatment is valuable, and, indeed, is the best preventive of diabetic coma, which is characterized as an acid intoxication of the blood, a true acidæmia. In the gastric crises of tabes this treatment has often been shown to be valuable, and as well in certain migraines known under the name of *gastroxie nerveuse*. In diseases of the heart and aorta, when this excess of hydrochloric acid coincides with hyposystole or asystole in mitral disease and in aortic affections, this remedy administered in massive doses has been followed by good results. In cutaneous diseases, especially in arthritic subjects, the condition of the blood is favorably influenced by this method. In disease of the liver and cholelithiasis, the alkaline treatment by Vichy water is well known, and especially when employed early and in large quantities is the cure rapid and successful.—*Revue générale de Clinique et de Thérapeutique*, 1893, No. 3, p. 35.

The Treatment of Myxœdema.

Mr. Robert Alex. Lundie believes that there are but few diseases so certainly amenable to treatment as this. A single case is reported. At first a real thyroid extract, representing two-thirds of a sheep's thyroid, was given hypodermatically, but as abscesses were caused, administration by way of the stomach was resorted to with equal success. Although this treatment always benefits the symptoms of the disease, yet it cannot be certainly said that it never does harm to the patient. Abscesses are by no means of infrequent occurrence when the remedy is introduced by the subcutaneous method. Other symptoms are due to later physiological effects, and have occurred after administration by the mouth. These may, in the main, be classified under the heads of—1. Weakness; 2. Pain; and 3. Nausea; all of which are mentioned as occurring in the case reported. Woodhead's experiments upon rabbits when he had injected various extracts of different glands showed that a marked effect upon the heart was produced, as very frequently degeneration of the muscular tissue ensued. It is certainly proper, then, to warn patients of the risk of unusual exertion, at all events in the earlier stages of the treatment. The author has collected from the literature a series of forty-six cases which illustrate the various methods of the administration of this remedy.

Dr. G. H. Melville Dunlap reports six cases, in five of which, all women, the treatment was successful. In the sixth, that of a man, there was not much evidence of improvement.

Dr. John Thompson reports a case which ended fatally shortly after the commencement of the thyroid treatment. A woman, aged fifty-one years, had certainly presented symptoms of this disease for ten years. For many months she had taken thirty minims of tincture of jaborandi three times

daily, to relieve the annoying dryness of the skin. Of late this had ceased to be a distressing symptom, and the drug had been discontinued. She had suffered constantly from more or less dyspepsia, from chilliness, and from a distressing feeling of weakness and disinclination for exertion. Five months before commencing treatment she was ill from a severe pain, which began in the region of the heart and passed down the left arm, accompanied by severe dyspeptic symptoms. This recurred frequently for a few weeks, and then passed off, though it returned occasionally afterward in a less severe form. During treatment, after unusual exertion, these symptoms returned, but were relieved by the administration of nitroglycerin. The symptoms of myxœdema were relieved, but she was very weak, and was sweating profusely; there was great nausea and much pain over the stomach. Later, this pain became more severe, and there was a constant inclination to vomit. Death occurred after suddenly fainting while sitting up. The necropsy showed that the muscular tissue of the wall of the heart was in a state of extreme degeneration, being pale and brownish in color and flabby in consistence, in many places being replaced by fibrous tissue, and in others by fat, owing to advanced atheromatous changes having obstructed the coronary arteries. The amount of thyroid used was certainly small (two and one-quarter sheep thyroids in three weeks), but one can scarcely doubt that it may possibly have had some influence in hastening the end. — *Edinburgh Medical Journal*, 1893, No. p. 996.

Treatment of Typhus Fever.

Dr. David Cerna advises perfect isolation in a well-ventilated room, scrupulous cleanliness, and thorough disinfection of all clothing and of the house. An absolutely healthy nurse, and one who has had typhus is to be preferred, should be selected, and he should have regular and proper nourishment and sleep and moderate alcoholic stimulation, especially by night. All utensils, before and after usage, must be thoroughly washed with boiling water; the hands of both nurse and patient disinfected with antiseptic solutions, and the vessels employed for the *dejecta* disinfected with great care. The alimentation should be of a liquid nature, chiefly of boiled cow's or goat's milk—two to two and a half pints in the twenty-four hours—to which tea, coffee, or orange-leaf water may be added. The free use of tea and coffee should be allowed, but in small quantities, frequently given. Later in the disease, and especially during convalescence, chicken and other animal broths, eggs, beef-tea, are given. The latter is administered twice a day—at noon and at night—with all due regularity. Fruit, such as baked apples, oranges, and the like, is sometimes allowed, with, of course, the necessary precautions. Care must be taken not to overload the stomach. Before and after the ingestion of food the mouth of the patient is thoroughly cleansed with a soft cloth moistened in a mixture of equal parts of distilled water and lemon-juice. Between meals the mouth may be washed with alkaline solutions. Thirst may be relieved by means of acidulated drinks. Above all, typhus fever requires a great deal of attention to be paid to alimentation, and the high mortality of epidemics is due chiefly to lack of proper nourishment. The treatment is mainly expectant, but the chief object is to keep up the

strength of the patient. Alcohol is one of the principal agents to be used from the outset. Good brandy, with sufficient sugar, in distilled water, to half a pint a day, or more, if the patient is unable to take food, is an efficient combination. Alcohol can also be used in the form of eggnogs and milk-punches. In the adynamic form other stimulants and tonics besides alcohol are often of great service. Ammonia, nux vomica, and quinine are indicated. If the nervous symptoms are prominent, accompanied by marked excitement and an elevated temperature, as in the ataxic type, these remedies are of little or no value, and may often do harm. If a condition, not of depression but of exhaustion, is present, nothing produces better results than the administration of musk in full doses. Constipation is the rule in this fever. This symptom, as well as the marked meteorism accompanying it, are combated chiefly by saline purgatives, preferrably the sulphate of magnesia, or by mechanical means. Calomel in fractional doses is sometimes employed for this purpose; cold-water enemata or glycerin suppositories are of use. Intestinal antisepsis is important; salol by the mouth and by the rectum is used, provided the kidneys are in good condition; also permanganate of potassium by rectal injection. Epistaxis is controlled by cold applications to the forehead. The catarrh of the stomach, a troublesome symptom at the commencement of the disease, is best treated by ipecac, other emetics being avoided, and food can be administered by the rectum. The severe headache, the delirium, and the insomnia are relieved by opiates, and particularly by the use of chloral. Hyoscine is sometimes used with good effect, especially in violent delirium. If the insomnia is without headache it may be relieved by valerian or camphor. The fever may be controlled by quinine if it occurs in exacerbations, as in malarial regions, or tepid baths cooled down to the required degree. In marked prostration, and when collapse is imminent, strychnine has been used with benefit.—*Medical Review*, 1893, No. 21, p. 403.

The Treatment of Disease without Alcohol.

Dr. B. W. Richardson, after an interval of a quarter of a century, returned to hospital practice at the London Temperance Hospital, taking charge of twenty-five beds. He reports his first two hundred cases occurring between April and October, 1892. His mortality was 14.50 per cent., against 11.60 per cent. on the medical side for the whole year of 1892, which he explains by the fact of the admission of all urgent medical cases and of many patients *in extremis*. The cases are far too briefly reported to indicate their severity, although in variety nothing more could be desired. Glycerin was used for making what might be called tinctures; various waters—aqua ferri, chloroformi, opii, quiniæ—were introduced; oxygen gas was used as a medium for carrying other volatile substances that admit of being inhaled with it—ether, ozonic ether, ammonia, amylene, amyl nitrite. He is satisfied that no aid which he could have derived from alcoholic stimulants, as they are called, could have bettered his results. He has acted on the principle of doing unto others as he would they should to him, and feels sure any candid medical brother who will have the steady courage to put aside many old and unproven, though much-practised methods, based only on unquestioning and unquestioned experience, and to move into these new fields of observation

and experience, will, in the end, find no fault with him for leaving a track which, though it be beaten very firmly and be very wide and smooth to traverse, may not, after all, be the surest and soundest path to the golden gate of cure.—*The Asclepiad*, 1893, No. 37, p. 1.

[The cases are too imperfectly reported and are too few in number to permit of any valuable conclusions. It is quite possible to conduct a hospital practice without resorting to any one of several commonly used drugs, as mercury, opium, digitalis, the iodides, quinine; but that fact would not prove that such practice was either advisable or proper. It is doubtless true that hospital physicians are likely to prescribe alcohol too frequently and with too free an hand; but abuse of a remedy is not an argument for its disuse and the deprivation of the unfortunate poor of a means that may tend to their relief. R. W. W.]

THE USE OF [MONO-] BROMIDE OF CAMPHOR IN VERTIGINOUS EPILEPSY.

DR. BOURNEVILLE has used this remedy for twenty years in the treatment of epilepsy when vertigo is a frequent complication. Five cases are reported showing the results of administration. The daily dosage is from three to seven capsules, each containing three grains of the remedy. Each week the daily dose is increased by one capsule until the maximum is reached, when the treatment is omitted for a week, to be resumed in the form of a daily dose of three capsules.—*Le Progrès Médical*, 1893, No. 18, p. 339.

THE TREATMENT OF CHLOROSIS BY IRON AND SOME OTHER DRUGS.

DR. RALPH STOCKMAN discusses the absorption, the stimulation, and Bunge's theory. He finds that there is overwhelming evidence that iron, when administered subcutaneously, will cure some forms of anæmia without even having had the opportunity of stimulating the alimentary canal or of neutralizing any possible sulphuretted hydrogen in the bowel. If given by this method, it is stored up in the liver chiefly, from which it is slowly excreted into the blood—probably in some organic combination—and no doubt thus subserves the gradual necessities of the organism. The dose is, however, small—one-half grain or less—and recovery is probably more rapid on larger doses given by the mouth. There may be some risk of irritating the kidneys, and no preparation thoroughly satisfactory for hypodermatic use has yet been proposed, and thus its exact value is somewhat difficult to gauge. Sulphide of iron, when administered to two patients, was followed by rapid recovery. In cases treated by the oxide, subnitrate, and salicylate of bismuth no improvement was observed in the condition of the blood until iron was substituted, when recovery took place rapidly. These three series of experiments are strong arguments against the theory of Bunge, that iron is only valuable so far as it absorbs sulphuretted hydrogen from the intestine. Arsenic has been used in chlorosis for many years, but the cases quoted show no reason to suppose that either the red corpuscles or the hæmoglobin are increased by its administration. If given with iron, it may be of benefit in so far as it acts as a gastro-intestinal tonic, improving the appetite and digestion, thus indirectly aiding in the cure. Also, by diminishing the demand of the tissues for oxygen, it may decrease the breathlessness of the

patient and thus add to her comfort. Manganese has a certain reputation as a hæmatinic, but in cases treated with the binoxide and sulphate, only the slightest improvement resulted. Hydrochloric acid may improve the digestion, but certainly not the blood condition. Purgatives, of themselves, do not cause improvement until iron is added, and the same is true of purely dietetic treatment, either alone or combined with out-door exercise or rest in bed.—*British Medical Journal*, 1893, Nos. 1687, p. 881; 1688, p. 942.

The Hyderabad Chloroform Commissions.

Dr. Patrick Hehir has carefully reviewed their work. The first Commission showed that the keystone to the safe administration of chloroform in man and in most of the lower animals is formed by the two principles enunciated in the following terms—(1) With regard to the heart: "The Commission consider that it is impossible for chloroform vapor to kill a dog by acting directly on the heart, and this holds good no matter in what doses or in what manner the anæsthesia is induced. Death from primary cardiac failure never took place. (2) Regarding the importance of watching the respiration: So long as the respiratory mechanism remains uninterrupted, chloroform anæsthesia is perfectly safe, but should the respiration be impeded and the elimination of chloroform be thereby interfered with, danger at once arises; in other words, if respiration be kept regular, no danger can arise." The essential object in view was to show that the principles upon which Syme administered chloroform were sound and reliable. Free admixture of air with the vapor of chloroform, which is insured by using some soft, porous material (as a towel or lint) presenting a large surface; no stint in the quantity of chloroform given; and watching the respiration. He considered that there was never any occasion to feel the pulse or examine the heart, either before or during anæsthesia. The second Commission brought out the practical points that (*a*) primary cardiac syncope during chloroformization does not occur; and (*b*) the maintenance of regularity of the respiration is absolutely indispensable to the safe administration of chloroform. By keeping the respiration regular the force of blood-pressure is kept regular also, as is likewise the action of the heart and the circulation generally. Under these circumstances it would be impossible to administer chloroform in poisonous doses unless it were continued after the occurrence of complete anæsthesia. A grand rule to follow in practice is to remove the chloroform and allow the patient to breathe fresh air for a second or two when at all in doubt.—*Medical Chronicle*, 1893, No. 1, p. 22, and No. 2, p. 73; and *Indian Medical Gazette*, 1893, No. 4, p. 103.

[This contribution is a most carefully written argument for the accuracy of the results obtained by these Commissions, and the practical points are worthy of the consideration of all who practise chloroform anæsthesia.—R. W. W.]

The Treatment of Primary Sciatica by Acupuncture.

Dr. E. Valentine Gibson reports that of one hundred consecutive cases treated by acupuncture, fifty-six were cured; thirty-two were much improved; ten were improved; while in two cases there was no improvement.

This is considered to be a very satisfactory result, considering the chronic nature and the severity of the cases. In addition to the acupuncture, they all used the Buxton thermal water, which has a great reputation for the absorption of inflammatory products. The needle should be single, spear-pointed and about two and one-half inches long. It should be inserted directly into the nerve, which will be known by the pain which shoots down the leg. The needle should be immediately withdrawn, as no better results are obtained if they are left *in situ*, and additional pain is likely to be caused. The nerve should be pierced about five times at intervals of a few days, over the parts where there is pain on pressure. Rest is necessarily most essential, as it is in other inflammatory conditions, and a rheumatic or gouty diathesis should be treated by appropriate remedies.—*Lancet*, 1893, No. 3633, p. 860.

Salophen.

Dr. Karl Osswald believes that in this remedy, which is a salol in which the poisonous phenol group is replaced by a harmless one—acetylpara-amidophenol—we have a substance which will present all of the advantages, with none of the disadvantages, of the salicylic acid preparations. As decomposition takes place in the small intestine, and as it is with difficulty soluble in cold water and is nearly tasteless, it does not destroy the appetite nor interfere with digestion. In small doses it is nearly entirely excreted by the urine; in larger doses, the excess is found in the feces. It does not cause untoward symptoms, even in a daily dosage of two drachms. It is less effective in the same dose than salicylate of soda, because it contains less salicylic acid. It can be used with advantage in mild cases of articular rheumatism, or as a substitute for the salicylate of soda when the latter drug is not well borne. In patients who present an idiosyncrasy against the salicylate of soda, and especially in debilitated individuals, or who suffer from sensitive stomachs, this drug can be used with advantage. It is useful in neuralgias of all kinds, especially in cephalalgias or hemicranias, in connection with chlorosis and anæmia.—*Deutsche medicinische Wochenschrift*, 1893, No. 16, S. 366.

Antipyrine in Diseases of the Urinary Organs.

Dr. J. H. Brik has found that this drug is a weak antiseptic, as is boric acid, and that it does not directly influence the reaction of the urine, but indirectly, through the nervous system, may render an alkaline or neutral urine acid. It is a useful analgesic in the purely nervous form of nephralgia and in the painful diseases of the pelvis and ureters, as inflammations and foreign bodies, etc. It is useful in the motor and sensory neuroses of the bladder, neck of the bladder and prostate, but it is of slight effect in inflammations, new growths, and tuberculosis of these parts. The hyperæsthesias and neuralgias of the urethra can be relieved by this drug. The best results are, however, obtained when the prostate or the prostatic urethra are involved. The property which this remedy possesses, similar to that of morphine, of acting upon unstriped muscular fibre, gives its field of usefulness in diseases of the urinary organs. It can be administered by the mouth or hypodermati-

cally, and in this way it is excreted by the kidneys, or by rectal injection or locally by injection into the bladder. If administered at night it is likely to relieve pain and produce rest. If ten to twenty drops of a 5 to 20 per cent. solution are injected into the prostatic urethra, a quite severe burning is apt to follow, which soon passes away, and is replaced by analgesia. This effect may last ten to twelve hours.—*Therapeutische Blätter*, 1893, No. 4, S. 97.

The Treatment of Gonorrhœa in Women.

Dr. Bröse treats acute cases by douches of chloride of zinc or sublimate, the urethra receiving 1 to 5 per cent. solutions of nitrate of silver by injection. In local treatment the cervix demands attention, and the application of strong solutions of chloride of zinc (to 50 per cent.) has been followed by the best results, although the practice is not without danger. Intra-uterine applications are likely to be followed by salpingitis and pelvic peritonitis, and are rarely necessary. Relatively dangerous is the washing out and injection of the uterine cavity with remedies designed to disinfect it; a harmless and proper method is the application of caustic remedies upon a sound wrapped with cotton, or in the form of pencils; or the method of Fritsch may be employed—mechanical dilatation of the uterus and packing the cavity with strips of gauze wet a with 2 per cent. solution of nitrate of silver, repeated daily for two weeks. The chronic urethritis is treated through the endoscope by a 5 to 20 per cent. solution of nitrate of silver.—*Deutsche med. Wochenschrift*, 1893, No. 18, S. 419.

Mercurial Inunctions and Sulphur Baths in the Treatment of Syphilis.

Dr. Josef Dymnecki presents an argument for the combined use of mercurial inunction and sulphur baths for patients suffering from long-standing syphilis. Although it is argued that the combination of mercury with sulphur is an insoluble one, yet the experience of the writer in treating thousands of cases at the sulphur springs of Busko since 1859 proves that this insolubility of the compound has no unfortunate influence upon the process of cure. The increased tissue change which goes on under the action of the sulphur baths apparently affords the mercury better opportunity to come in contact with the syphilitic poison in the various organs, and thus this combination is favorable for a speedy cure.—*Internationale klinische Rundschau*, 1893, No. 18, S. 671.

The Antiseptic Value of Phenocoll Hydrochloride.

Dr. Carl Beck presents a preliminary communication, giving the results of his experiments with—*a*, the pure powder; *b*, 5 per cent. watery solution; *c*, 10 and 15 per cent. alcoholic solution; *d*, 10 and 20 per cent. gauze; *e*, 10 and 20 per cent. ointment. The pure powder does not irritate, and the healing process does not differ from that observed under iodoform. Repeated examinations of the urine revealed nothing abnormal. The 5 per cent. watery solution was successful in dermatitis, erysipelas, gonorrhœa, leucorrhœa. The 10 per cent. alcoholic solution was injected into the joints of hip

and ankle without irritation, but the final result was doubtful. The injection of a watery, and especially of an alcoholic solution, was always followed by a slight, transitory burning sensation. The 20 per cent. ointment (preferably made with lanolin) was used for an ulcer of the leg and for burns of the second degree. The granulations were of good character, but the healing process seemed to take longer than it did under the use of the gauze. This remedy is probably as valuable an antiseptic as iodoform, and is stronger than dermatol, aristol, iodol, pyoktanin, or europhen. It probably surpasses iodoform, because—1, it is odorless; 2, it dissolves easily; 3, it does not produce eczema; 4, it is not contra-indicated in kidney disease; 5, on account of its non-poisonous effects it can be applied to very extended surfaces. As a very small amount of the drug fulfils its purpose, the expense is small.—*New York Medical Journal*, 1893, vol. lvii., p. 438; *Notes on New Remedies*, 1893, No. 11, p. 177.

The following papers are worthy of notice:

"The Treatment of Malaria," by Dr. M. T. Schuiret, in the *Wiener medizinische Presse*, 1893, No. 13, p. 492, and No. 14, p. 535. A very careful review of the recent literature of quinine, phenocoll, methylene blue, helianthus annuus [sunflower], nitrates of soda or potash, alum, and hydrotherapy.

"Neurology and Therapeutics," by Dr. William R. Gowers, in the *British Medical Journal*, 1893, No. 1685, p. 781; No. 1686, p. 833; and the *Lancet*, 1893, No. 3633, p. 849.

MEDICINE.

UNDER THE CHARGE OF

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Hereditary Enlargement of Spleen.

Wilson made a further communication to the Clinical Society of London (April, 1893) on some cases of hereditary enlargement of the spleen. The previous communication was in 1890. The possible malarial origin was finally abandoned. While, as regards the hereditary element, the cases were unique, they resembled in many important particulars some of the cases described under the term "splenic anæmia," "primitive splenomegaly," etc. All the cases in this series had occurred in adults, had run a more or less protracted course, and presented the following clinical characters: (1) Enlargement of

the spleen without any corresponding enlargement of the glands; and (2) marked globular anæmia without leucocytosis. In some of the cases there had been fits of epistaxis, and in others febrile attacks, accompanied apparently by active destruction of the red blood-corpuscles. It was suggested that, for temporary purposes at least, the series might be usefully regarded as a single group, and that the name "chronic splenic cachexia" appeared the most suitable under which to describe cases possessing these characteristics.

Rapid Pleural Effusion.

White (London) relates the following case (*Lancet*, 1893, No. 3630):

The patient had ordinary tubal nephritis together with mitral constriction and regurgitation. On December 16th, 36 ounces of fluid were withdrawn from the right chest. Next day there was excruciating pain in this region and 106 ounces were withdrawn (thirty hours after the first tapping). Seventy-eight hours later 120 ounces were removed from the same side. On this occasion there was again intense pain and dyspnœa and great œdema of the neck, probably due to the pressure on the superior vena cava. Thirty hours later 50 ounces were removed.

"It seems to me that the only possible explanation of this extraordinarily rapid accumulation of fluid is that the patient had thrombosis of her large azygos vein before it is joined by that from the left side. It is not against this view that we saw no enlarged superficial veins, for the most important anastomoses between the branches of the azygos veins of the two sides and the large azygos vein and the inferior vena cava are deep-seated in the abdomen, the thorax, and around the spine. Nor is it conclusively against this supposition that no evidence of thrombosis was found post-mortem, for the patient did not die till eight weeks afterward, by which time all signs of thrombosis might very well have disappeared. She had the clinical symptoms of thrombosis of her femoral vein only ten days before her death, and yet the vein was at the necropsy found to be patent. I have often observed that when patients have died no evidence has been forthcoming of thrombosis although all the signs of it have been present during life. It seems to me that no other explanation offers itself of this case, in which, supposing the fluid collected at a uniform rate, after the first tapping of the right chest that rate was three ounces and a half per hour, after the second one ounce and a half per hour, and after the third about one ounce and a half per hour. It is also quite exceptional for the distention of the chest with fluid to be so rapid as to cause acute pain, and it is no doubt comparable to the severe pain in the calf, felt in acute femoral thrombosis, and, like it, is probably due to the rapid stretching of the parts by the fluid; also it must be very rare for the pressure of the fluid in the superior vena cava to cause œdema of the neck."

Vesicular Eruption on the Palate: a Sign of Influenza (?).

Shelly draws attention (*Brit. Med. Journ.*, 1893, No. 1685) to a peculiar appearance of the soft palate. When examined in a good light it was found to be more or less completely studded with minute, translucent, lenticular

elevations, somewhat resembling tiny, well-boiled grains of sago. The size was usually 0.5 mm., never exceeding 1 mm. in diameter.

"These vesicles were most abundant about the soft palate above the root of the uvula; but in some cases—and these were generally of the more severe type—they occupied a much larger area, being visible over the greater part of the roof of the mouth, but being always most marked and most abundant in the situation first mentioned. The patient was quite unconscious of and apparently unaffected by their existence.

"I was, of course, aware that the condition described is to be observed in cases other than those of influenza; nor do I yet venture to suggest that it is pathognomonic of that disease. No one can examine the throats of a large number of persons without occasionally observing the presence of these vesicles, to some extent at all events; but in connection with no other malady had I noticed them to be, not merely so frequently, but constantly, present, and this from the earliest period of the illness and throughout convalescence."

In the summer of 1891 abundant vesicles were noted in the case of every boy admitted to the Sick House at Haileybury College. Whenever, during that epidemic, vesicles were observed in boys who reported themselves on account of trivial injuries or other ailments, they were immediately sent to bed, and in one only out of forty did indubitable symptoms of influenza fail to develop within twenty hours. Of seventeen boys who—though complaining of malaise and exhibiting some pyrexia—did not present any abnormality of the palate, five only subsequently developed influenza.

These vesicles appear in all forms of the malady, but perhaps more conspicuously in the cases in which the respiratory passages are especially implicated. They persist throughout convalescence.

Raw Pancreas in the Treatment of Diabetes.

White (London) records the following results (*Brit. Med. Journ.*, 1893, No. 1679). Two cases were submitted to treatment. Each patient was for the whole period of observation kept upon a diet consisting each day of twenty Soya-bean biscuits, two eggs, two ounces of butter, two almond biscuits, one fluidounce of milk, twelve ounces of cooked meat, greens, watercress, tea, and soda-water. The state of the patients and of the urine on this diet having been ascertained, each was given in addition, for his supper, about two ounces of raw fresh sheep's pancreas chopped fine and flavored with pepper and salt. When this was discontinued five minims of liquor pancreaticus were injected subcutaneously night and morning, the restricted diet being as before.

As regards the sugar, in one case it was distinctly less when raw pancreas was taken than it was before, and the same effect, but to a less degree, was associated with the injection of liquor pancreaticus subcutaneously. In the second case, neither of these methods had any effect in reducing the sugar.

Quantity of urine. No decided effect observed, nor was the specific gravity appreciably affected.

Urea. No effect was produced on this in Case 1. Possibly an increase was due to the treatment in Case 2.

General effects. The patients liked the raw pancreas. They did not lose weight on it; if anything, there was a slight improvement in their condition.

Disadvantages. In one case severe erythema with fever; in the other, sore-throat with rise of temperature.

White thinks it very doubtful whether any benefit is to be expected from this treatment of diabetes mellitus.

Hereditary (Friedreich's) Ataxia.

Senator (*Berliner klin. Wochenschr.*, 1893, No. 21) has reported a case of hereditary (Friedreich's) ataxia in a male, nineteen years old. Awkwardness of gait had been observed during childhood, and had grown progressively worse. Intelligence was preserved; static ataxia was marked; the gait was unsteady; the knee-jerks were enfeebled and inconstant, even with reinforcement. Vertigo was complained of. Sensibility was normal, and there was no distinctive trophic change. There was a slight degree of horizontal nystagmus, but no other ocular symptom. The tongue occasionally presented slight fibrillary contractions. Speech was slow, drawling, and impeded, somewhat monotonous, but not scanning. The function of the sphincters was not deranged. A sister of the patient, thirty-two years old, had also presented similar symptoms from childhood. Senator does not agree with the view that ascribes the pathology of hereditary (Friedreich's) ataxia to combined sclerosis of the posterior and lateral columns of the spinal cord. He believes that the primary lesion is a congenital defect in the development of the cerebellum or of physiologically related parts in the medulla oblongata, and points out the close similarity between the symptoms of hereditary (Friedreich's) ataxia and those of cerebellar disease.

A Case of Pulmonary Syphilis.

Jullien (*Annales de Dermatologie et de Syphilographie*, tome iv., No. 4, p. 45) has reported the case of a woman, forty-six years old, who presented herself with ulceration and tumefaction of the right leg, that had existed for a year, and was painful and impeded the gait. The appearances were those typical of syphilis; besides, the tibia was found to be swollen. The woman had borne three healthy children by a first husband; her second husband was also dead, and had probably been syphilitic. The woman was greatly emaciated, extremely pale, and presented a cachectic appearance. For several months she had had constant fever, with vesperal exacerbations and night-sweats. The breathing was difficult, shallow, and rapid; cough was almost incessant. The expectoration was copious and muco-purulent. On physical examination, irregularly distributed areas of impaired pulmonary percussion-resonance were found, of greater extent and degree upon the left, with harsh breathing and fine and coarse moist and dry râles—in a word, the signs of infiltration and softening in various parts of the lungs. Careful and repeated examination of the sputum failed, however, to detect the presence of tubercle bacilli. Numerous animals inoculated with the sputum died of septic abscess formation, but none of tuberculosis. The woman was, besides, a pronounced dyspeptic, with marked gastrectasia. She was placed upon general tonic and constructive treatment, given potassium iodide by enema in milk, and subcutaneous injections of calomel. The improvement was so decided in the

course of seven months that, notwithstanding admonition to the contrary, the woman withdrew from treatment. Her condition again became worse, but on resuming treatment pronounced improvement again took place. The results of physical examination now indicated retrogressive changes in the lungs. The woman, however, again became worse, anæmia and emaciation becoming marked, and hæmoptysis being so profuse as to threaten life. A course of injections, according to the method of Brown-Séquard, was now instituted, with results that exceeded anticipations.

The Bacteriologic Diagnosis of Cholera.

The following is the mode of procedure carried out at the Institute for Infectious Diseases at Berlin, in a bacteriologic study of a suspected case of cholera (*Zeitschrift f. Hygiene u. Infectionskrankh.*, 1893, Bd. xiv.; *Deutsche medicin. Wochenschrift*, 1893, No. 22, p. 523). Cover-glass preparations are first made (the flakes of mucus that are often present in the dejecta being selected) and stained with a dilute carbolized fuchsin solution. If comma bacilli be found, peptone cultures and gelatin plate-cultures are made. The peptone medium consists of a sterilized one per cent. watery solution of peptone and of sodium chloride, to which sufficient soda is added to impart a decided alkaline reaction. This is kept at a temperature of 37° C. If cholera bacilli are present in large number, a pure culture will be found on the surface of the peptone solution at the end of six hours; if present in smaller number, the culture will develop more slowly and there will be an admixture of other bacteria. It is best to look for the bacilli in from six to twelve hours after inoculation. If the peptone contain a certain proportion of nitrates, if the sulphuric acid employed be free from nitrous acid, and if the cultures be pure, the cholera-red (indol) reaction will take place. A good ten per cent. gelatin culture-medium is inoculated and kept at a temperature of 22° C. At the end of from fifteen to twenty hours characteristic appearances will have developed. If upon primary microscopic examination cholera bacilli have not been found, agar plates are cast in addition to the inoculation of the peptone solution and the gelatin plates. Six hours after the inoculation of the peptone solution curved bacilli are from time to time looked for; and as soon as found agar plates are cast. The material to be examined is preferably not mixed with liquefied agar; but the sterile agar is permitted to harden in covered dishes and placed for a few days in the thermostat to permit the expressed water to evaporate. The surface of the agar is then inoculated with the suspected material or from the peptone solution and kept at a temperature of 37° for eight or ten hours. If cholera bacilli be present they form colonies of light-yellow, transparent appearance. If few cholera bacilli have been found in the peptone solution and few or no colonies on the gelatin plates, suspicious or doubtful colonies upon the agar plates must be transferred to other agar plates, to peptone solution, and to gelatin plates, so that sufficient material may be obtained for the purposes of the indol reaction and of experiment upon animals. For this last purpose, cultures from the surface of agar plates are to be preferred. With a platinum loop, about 1.5 mg. of the culture are taken and mixed with 1 c.cm. of sterilized bouillon and injected into the peritoneal cavity of a guinea-pig. This

is lethal for a pig weighing from 300 to 350 grammes. The peptone solution may also be employed for the detection of cholera bacilli in water. To about 100 c.cm. of the suspected water are added one per cent. each of peptone and sodium chloride and the mixture is kept at a temperature of 37°. In ten, fifteen, and twenty hours agar plates are to be inoculated with this solution. The resulting colonies are further cultivated upon peptone, glycerin, and agar, studied for the indol reaction, and injected into lower animals.

Tuberculosis of the Buccal Cavity, with Perforation into the Nares and Maxillary Antrum.

Rethi (*Wiener medicin. Presse*, Jahrg. xxxiv., No. 19, p. 721) has reported the case of a man thirty-one years old, without history of syphilis and without hereditary predisposition, who for eight years presented cough, with mucous expectoration, at times blood-streaked. In 1888 there appeared pain in the throat, particularly upon swallowing, together with hoarseness and cough. Some improvement in these symptoms took place, but they returned in the course of the following year. Examination now disclosed the evidences of a tuberculous process at the apex of the left lung and in the larynx. Matters grew gradually worse and in time the right lung also became tuberculous. The man's condition fluctuated for a couple of years, until, after the removal of a tooth and several roots, the opening left in the gum would not close and there resulted an ulcer, attended with considerable secretion. In the hope of effecting a cure other teeth were sacrificed and some fragments of bone were thrown off spontaneously. Little change took place in the process in the larynx, but that in the lungs steadily advanced. Histologic examination of a bit of tissue removed from the mouth in the neighborhood of the ulcerated area, disclosed the existence of a tuberculous process, round-celled infiltration, with epithelioid cells and giant cells, and in the midst of which a small number of tubercle bacilli were visible. The process advanced in spite of persistent treatment. Early in 1891, the left naris became occluded and soon afterward a communication was observed to have taken place between the mouth and the nares and the antrum of the upper jaw. Almost all of the upper teeth on the left side were gone, and the alveolar margin and the adjacent hard palate were destroyed. Difficulty in swallowing (fluids and solids entering the nares) and in speech rendered necessary the wearing of a plate of artificial teeth. Cauterization, curetting, applications of lactic acid, and other treatment proved of no avail. The glands behind the left sterno-mastoid muscle became enlarged and a cold abscess formed and had to be evacuated. The communication between the mouth and the nose finally extended from the left second molar tooth almost to the middle line, along the alveolar margin to the right second incisor and backward to the last molar, the roots of which were exposed. The under surface of the septum narium was exposed and the ulcerated, granular and purulent surface of the mucous membrane of the antrum was also to be seen. This condition of affairs continued until interrupted by the occurrence of death. It is an interesting question whether the tuberculous process in the mouth was secondary to the extraction of the tooth, or if such a process was the primary factor that led to the loosening of the tooth.

A Remarkable Traumatic Neurosis.

Pel (*Berliner klinische Wochenschr.*, No. 24, p. 561) has reported the case of a man, twenty-seven years old, who fell a distance of two stories, possibly striking his head. Consciousness was lost and did not return for four hours, when severe headache appeared, referred particularly to the nape of the neck and the occipital region upon the left side. There was neither nausea nor vomiting, nor hemorrhage from the nose or ears, nor involuntary passage of urine or fecal matter. No external lesion could be discovered. The patient remained in bed for three days, complaining of left-sided occipital headache, vertigo, and drowsiness. Weakness of the right side of the body was also observed. Speech was not interfered with, but standing and walking were performed only with difficulty. On attempting to resume his occupation as a carpenter, after the lapse of four weeks, the man found himself unable to do so on account of headache, vertigo, and a sense of fatigue in the extremities, especially those of the right side. In the course of time vision became impaired and the other symptoms became aggravated, until, ten months after the accident, the patient was unable to stand or walk. In the recumbent posture, however, he had perfect control of the movements of the lower extremities, but as soon as an attempt was made to place him upon his feet the lower extremities would give way and the patient would fall unless supported. The knee-jerks were exaggerated. The face at the same time became red, and the skin covered with perspiration; the pulse increased in frequency, and the patient appeared as if exhausted. On examination a complete right-sided hemiparesis was found to exist. Common and special sensibility were normal, and there were no muscular or cutaneous trophic changes. The urine presented no abnormality. Upon laryngoscopic examination a polyp was found seated upon the anterior portion of the right vocal band, and which, upon phonation, became incarcerated between the two bands. A high degree of myopia existed, but there was neither choked disk, optic neuritis, limitation of the field of vision, nor disturbance of the color-sense. There was no neurotic or psychotic family history, and no personal history of alcoholic or venereal excesses. The diagnosis wavered for a time between functional derangement of the central nervous system—traumatic neurosis and organic disease of the cerebellum—tumor, cyst, abscess. It was determined to remove the polyp in the larynx, and immediately after the operation the man became aphonic. In the course of several weeks there developed right-sided hemianæsthesia, hemianalgesia, hemianosmia, hemiamblyopia, and bilateral loss of the sense of taste. A little later all doubt as to the diagnosis was removed by the occurrence of an hystero-epileptic attack, and some time later a second attack. In spite of assiduous treatment the condition of the man underwent little improvement. He was finally attacked with bilateral catarrhal pneumonia, to which he rather unexpectedly succumbed. A careful post-mortem examination failed to disclose any organic change to explain the symptoms present during life.

SURGERY.

UNDER THE CHARGE OF

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THE VALUE OF INTERNAL MEDICATION IN THE TREATMENT OF MALIGNANT DISEASE.

IN discussing the treatment of malignant disease by internal medication, WRIGHT (*Annals of Surgery*, April, 1893) does not uphold this method to the exclusion of surgical interference, but rather advises its use in preparation for and in conjunction with the most thorough extirpation by the knife. For the purpose of destroying outlying foci of disease left by the knife, he tried various drugs internally, and in cases that he had operated upon, as well as in those in which operation was impossible, he began to give the bromide of arsenic in one-fortieth to one-tenth grain doses after meals, and the carbonate of lime before meals in five to ten-grain doses in the tincture of calumba. In many cases coming under the head of sarcoma, there was quite a rapid tendency toward cure, and this was generally permanent. Large deposits, as a rule, would not yield, but excision of the enlargement was often followed by a sure cure. As to cases affecting bone, osteo-sarcoma, the treatment was not so favorable, but seemed of some value. He advises practitioners to give the bromide of arsenic to all patients as soon as they come under their care, and continue the remedy for a long time after operation. In a considerable number of cases operated upon for cancer in the past three, four, and five years, to whom the bromide of arsenic was administered for a time, say six or twelve months, complete health has been restored and the scar tissue is now in every way just as normal as it would be if the wound had been in perfectly healthy tissue. In no case did the microscopic examination fail to confirm the diagnosis. The same results might possibly have been obtained by complete and thorough operation, and yet he believes there is value in the after-treatment, and that a case would be neglected without it. In inoperable cases he has seen good results, not the removal of the growth, but relief of pain and a retardation of the growth. In some cases of cancer of the intestines he has seen the bromide of arsenic bring relief and prolongation of life.

THE USE AND PLACE OF CAUSTICS IN THE TREATMENT OF CANCER.

LEWIS (*Annals of Surgery*, 1893), in discussing the use of caustics, agrees with the principle of Walshe, who said: "Escharotic agents should be

applied in such a manner as to produce the requisite effect, if possible, by a single application, otherwise the irritation gives, not necessarily but commonly, new activity to the disease." The dangers of mild cauterization are only too frequently seen. Caustics in operable cases, as cancer of the breast, should never be preferred to the knife. Caustics should not be used in cases involving any mucous surface. In cutaneous cancer the author finds a field for the use of caustics. He says: "The disease can be thoroughly destroyed by caustic applications, which act sufficiently upon the diseased tissues without destroying the healthy skin." "The resulting cicatrix, when the deep subcutaneous tissues are not involved, is a smooth, white, and in every way healthy one, and far less conspicuous than those remaining after operation." The only exceptions he finds in cases involving the mucous surfaces of the lips or eyelids or a large surface. If the disease is a small, warty growth, he advises the use of Jennings' potash and cocaine paste. The formula is as follows:

R.—Hydrochlorate of cocaine	2 parts.
Caustic potash	12 "
Vaseline	6 "

Acetic acid must be at hand to limit its action as soon as desired. He has used in over one hundred cases a paste recommended by Marsden, composed of arsenous acid, two parts, and mucilage of acacia, one part, mixed into a paste too thick to run. It is not to be used in cancers more than four square inches in area, and is to be applied to only one square inch at a time. It should be covered with absorbent cotton to absorb superfluous paste, and left on till some swelling of inflammatory character appears around the border of the plaster, when it is removed. From one to three days are required to produce the desired effect; then warm poultices are applied to remove the slough, and a healthy ulcer follows, which heals rapidly. Bougard's paste, which is less painful, is used in a similar manner, but can be applied to a larger surface, and kept prepared in a covered jar. The skin surface must be removed with caustic potash in both cases. Bougard's formula is as follows:

R.—Wheat flour	60 grammes.
Starch	60 "
Arsenic	1 "
Cinnabar	5 "
Sal ammoniac	5 "
Corrosive sublimate	0.50 centigramme.
Solution of chloride of zinc at 52° F.	245 grammes.

The Domain of the Knife in the Treatment of Carcinoma.

Jacobson (*Annals of Surgery*, 1893) believes that in the knife we have the only means of dealing with cancer, and to be effectual the operation must be extensive, thorough, and painstaking; all diseased tissues, and every suspected portion of tissue must be removed, and every lymphatic that communicates with the diseased area, whether infected or not. The present status of belief in this regard is not that such a radical removal is best, but that it must be done, and is indicated in every operation no matter how small the area of

infection may be. In breast operations the axilla must always be thoroughly cleared of all glands and fat; if the glands show evidence of infection, great care should be taken to remove all vestiges of the disease; the danger of leaving foci on the pectoral fascia is great, and all the fat should be carefully removed, while some authors go so far as to advise the removal of a layer of the pectoral muscles. Thorough removal is preferable to immediate union and complete coaptation. In cancer of the uterus the difficulties are greater and recurrences more frequent, but the more radical and complete the operation the greater are the patient's chances, provided an operative recovery is not endangered. Methods are still unperfected, but with improved technique in operating the author believes that the knife will remain in the future, as it is now, the best means of treatment at our command. Early diagnosis and operation are important factors in reducing the mortality. In conclusion the author says: "I may be permitted to reiterate that recent study of cancer only emphasizes its infectious character and primarily local origin. To effect its cure we must be able to reach beyond the infected area into healthy structure. To accomplish this with reasonable certainty the surgeon has but one agent—the knife."

A New Indication for Perineal Urethrostomy; Extensive Destruction of the Urethra.

Poncet (*Gaz. hebd. de Méd. et de Chir.*, 1893) reports a case of extensive laceration of the urethra in which he deemed it necessary to make a perineal section in order to drain the bladder and prevent urinary infiltration, infection, and consequent sloughing. The patient passed into his urethra a large cord, using a twisting motion in order to make it enter. This peculiar motion had the effect of tying a knot in the cord at a point either within the bladder or in the prostatic urethra. When the patient found himself unable to withdraw the cord he cut it off close to the glans, the end slipping back within the urethra. It remained in this position, the patient urinating around it, for two weeks, and seemingly produced no distress or pain until the end of that time, when the patient came into the hospital with an enlarged and inflamed organ. The cord was extracted with difficulty with urethral forceps, but the subsequent inflammation was so intense that a perineal urethrostomy was necessary. The patient recovered, but the urethra had been so effectually destroyed that it was impossible to re-establish its function.

A Case of Perineal Lithotrity.

Bangs (*Annals of Surgery*, 1893) reports a case in which he performed supra-pubic cystotomy, removing a stone weighing 400 grains, and two protruding portions of the lateral lobes of the prostate. Siphon drainage was employed in the usual manner. The patient recovered, but had little control over the bladder. Urination was painful, frequent, and complete evacuation was impossible except by the use of the catheter, and at his best he was compelled to urinate every two hours. This condition continued for two years; treatment by rest and washing out the bladder affording some relief. Finally, after an aggravated attack, a stone was found, and incrustations on

the anterior bladder wall. The author decided to perform perineal lithotrity, or Dolbeau's operation. By means of a staff and the use of Dolbeau's dilator a canal of from one to one and a half inches was tunnelled through the perineum and prostate, the lithotrite introduced, and the stone crushed and removed. A drainage-tube was introduced, the wound packed with iodoform gauze, and siphon drainage maintained for four weeks, when the tube was removed, and the wound healed in eleven days. The expulsive power of the bladder was quickly regained, and the patient urinated standing. The interval varied from four to six hours, and at night seven to nine hours. The author believes the improved condition to be due to the great dilatation of the prostatic urethra.

The Radical Cure of Hernia by Bone Plates.

Thiriar (*Le Merc. Méd.*, 1893) describes a new method for performing this operation, which he has used successfully in twenty-five cases. It consists in the interposition of a decalcified bone plate, larger than the internal ring, between the abdominal parietes and the peritoneum which has been dissected up from the inner surface, around the stump of the previously ligated hernial sac. The bone plate is held in position by sutures that are so placed as to approximate the different layers of the abdominal wall. In the twenty-five cases which the author operated upon he has seen no relapses and no failures, and the cases upon which it has been tested have been the most unfavorable ones which have come under his care; in some cases relapse had occurred after other attempts at radical cure; in others the herniæ were very large, and the abdominal opening would admit three or four fingers, while the tissues were weak and relaxed. The part that the author ascribed to the bone plates is that of a structure upon which the leucocytes could build up a dense mass of connective tissue following gradually as the bone plate was absorbed. This he was able to prove by microscopical examinations of pieces that were thrown out of the wound unabsorbed. The production of this thick mass of cicatricial tissue produces a plug that does not yield to pressure. The bones used by the author were the shoulder-blade or any of the large bones of the beef or porker. They should be taken as the animal is killed, denuded of their periosteum, without injury to the bone substance, and plunged into a 10 per cent. solution of hydrochloric acid. The amount used should be ten times the volume of the bones, and should be renewed every two days. The action is more rapid if the bones are cut into small pieces; they are sufficiently decalcified when soft and pliable under water, without the production of bubbles. The marrow of long bones can be removed the second or third day. It is then placed in a 1 : 1000 bichloride solution for two days, and finally preserved in an ethereal solution of iodoform, but must be dehydrated in 95 per cent. alcohol previously.

Loose Bodies in the Knee-joint.

Richardson contributes (*Boston Medical and Surgical Journal*, 1893, No. 21) some valuable suggestions on this subject. As is well known, opening of the knee-joint has always been attended with considerable risk. Under Listerian methods this risk has been very much reduced, but it undoubtedly

still exists, as cases which have been operated on with the most careful attention to antiseptic detail have occasionally resulted in the destruction of the joint, and even in death from septicæmia. The annoyance caused by foreign bodies in the knee-joint is so considerable in many cases that operation seems demanded.

Attention to the following recommendations of the author will no doubt render this operation as free from danger as other surgical procedures of like magnitude. Every detail of asepsis is to be carefully carried out. It is advised to open the supra-patellar pouch external to and above the patella. If possible, the loose body is to be grasped between the thumb and forefinger of the left hand, and thus held while the incision is being made. Before opening the synovial membrane, all bleeding-points must be secured with pressure forceps. The hands of the operator and of his assistant should not come in contact with the wound. The cut surface is kept dry with *dry* sterilized gauze held in forceps. The flaps are kept retracted with vulsellum hooks. Having dried the wound, the synovial membrane is cut through, the foreign body grasped with forceps and withdrawn. Avoid digital exploration, and do not irrigate the joint, unless there has been a large effusion present.

The author prefers to close the wound with silver wire armed with a needle at either end, so that the punctures through the skin may be from within out. The wound is sealed with iodoform collodion; a posterior splint and antiseptic gauze and cotton are applied with gentle pressure.

Four cases are reported in which the result of the operation was satisfactory.

Separation of the Lower Femoral Epiphysis.

Mayo Robson reports (*Annals of Surgery*, 1893, No. 1) three cases of this accident coming under his care. Attention is called to the fallacy of considering these injuries as equivalent to transverse fractures of the lower end of the shaft of the femur, and of treating them as such, as is recommended in most text-books.

In two of the cases reported the separated epiphysis was dislocated forward, the lower end of the diaphysis projecting in the popliteal space; the affected limb was shortened. In the third case the separation was incomplete. The deformity in this case was but slight, save the swelling of the joint, and the affected limb was somewhat longer than its fellow, measured from the anterior superior spine of the ilium to the lower border of the patella. In three other cases observed by the author the dislocation was forward in each instance.

Reduction is to be accomplished, under anæsthesia, by extension, counter-extension, and manipulating the epiphysis into position. For retention, the posterior splint, the double inclined plane, or the long splint, with weight and pulley, may be employed.

In the cases recorded a perfect recovery took place in every instance, without any impairment of function.

Nearly all of the reported cases have been caused by direct violence. The direction of the displacement will be determined, at least in part, by the direction in which the violence has been applied, and also upon the attach-

ment, or otherwise, of the gastrocnemius tendon to the lower end of the upper fragment.

The diagnosis in most cases is not difficult. Shortening of from one to two inches, the projection of the lower end of the diaphysis in the popliteal space, the displacement of the epiphysis on the front of the femur, and the interference with the circulation of the leg, when taken together with the cause of the injury and the age of the patient, form, according to the author, a group of symptoms pathognomonic of the injury under consideration.

If reduction is impossible, excision may be resorted to; while, if the great vessels have been ruptured, or gangrene has occurred, amputation must be performed.

IODOFORM IN THE TREATMENT OF TUBERCULOSIS OF BONES AND JOINTS.

BRODNITZ claimed (*Deutsche Zeitschr. f. Chirurgie*, Bd. xxxv., Hefte 5 u. 6) that the results of operative treatment of bone and joint tuberculosis have considerably improved since the employment of iodoform has been practised. KÖNIG explains this by assuming that tuberculosis cannot develop in quickly contracting scar tissue. Mosetig v. Moorhof attributes a specific effect to the iodoform.

For the past three years the author has used iodoform, as recommended by Billroth, which consists of a sterilized 10 per cent. mixture with glycerin. The absolute sterilization of the mixture is of the utmost importance.

The author reports 20 cases of cold abscess subjected to this treatment. Of these 9 were cured, 8 had fistulæ remaining, and 3 were unheard from. Of 25 cases of bone tuberculosis operated upon, and the iodoform-glycerin mixture employed in addition, 20 were discharged cured. Nine cases of capsular tuberculosis were subjected to arthrectomy and the use of iodoform, and 7 were definitely cured.

DE VOS has written an exhaustive monograph on this subject (*Centralblatt für Chirurgie*, 1893, No. 3). He prefers the iodoform mixed with olive oil, and carefully sterilized. It is used in exactly the smae manner as the iodoform-glycerin mixture.

Seventy-two cases are reported, which have been subjected to this treatment; 72 per cent. of these are said to be entirely cured. The duration of the treatment in the different cases was from 9 to 325 days. The number of injections ranged from one to twenty. The amount of iodoform used was from 2 to 67.5 grammes, and of oil, 10 to 385 grammes.

Improvement is shown, after beginning this treatment, by decrease of the pain and of the swelling; and new connective tissue results at the seat of the injections. This latter is said to have been observed in a patient whose knee-joint was resected after having undergone the iodoform treatment.

OBSTETRICS.

UNDER THE CHARGE OF

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SYMPHYSIOTOMY.

SWIECICKI (Posen) reports (*Centralblatt f. Gynäkologie*, 1893, No. 23) a case aged twenty-one years, I-para, with a flat and generally contracted pelvis; conj. vera, 7¾ cm. Symphysiotomy; child delivered with forceps; recovery after four weeks.

NEUGEBAUER, in 196 new operations for symphysiotomy, from 1827 to 1893, found that there were 23 deaths. Of these, 4 were from causes not connected with the operation, and in 19 cases the death was in relation with operation.

SCHAUTA believed that more symphysiotomies were prepared for than were done, the birth ending by the application of the forceps. The wounding of the soft parts came not through the transverse but by the longitudinal stretching of the head. He holds the hand to be the best means of protecting the soft parts.

ZWEIFEL regards symphysiotomy as an acquisition to surgery, and considers that it will become of much more importance than Cæsarean section in the universal practice of the surgeon. By waiting for spontaneous birth after the operation we avoid the wounding of the soft parts and of the child by the forceps.

He mentions two cases; one with the conjugate of 8½ cm. He believes the bad after-history to be often due to bad, defective adaptation and no sewing of the joint. He has always drained the wound. The forceps should always be first tried.

KEIN (*Gaz. de Gyn.*, 1893, No. 16) reports a case of symphysiotomy in a multipara during the third day of labor. Pelvis narrowed by fibroids of sacrum and pubis. Conj. diam, 6½ cm.; conj. ext., 18 cm.; vaginal secretion purulent. After division the pubic bones separated ¾ cm., and a living child was easily extracted with the forceps, the bones separating to 7 cm. during traction. Hemorrhage slight. Woman made a good recovery, although two abscesses formed at ends of incision.

V. COCQ (*Journal de Medicine, de Chirurgie, et de Pharmacologie*, 1893, vol. ii., p. 97) gives his conclusions on the operation of symphysiotomy, as follows: Mousan puts the pubic separation at 7 cm.; Pinard at 6 cm. For each centi-

metre of separation the pubo-promontory measure increases on an average 2½ mm. The maximum separation at section with safety to the sacro-iliac joint is about 6 cm., the increase of the sacro-pubic line will then attain about 13 to 15 mm. He further concludes:

1. It is easily performed, and requires only the usual surgical outfit.

2. It is an operation of urgency that everyone should be able and ready to perform—like tracheotomy.

3. The operation is legitimate only with strict antisepsis.

4. A pubic separation of 6 cm. is without danger and equals 22 mm. antero-posterior diameter.

5. It is advantageous to mother and child, and the mortality is small.

6. After forceps and version have been tried, operate if child be living, and the superior conjugate diameter be 6.7 cm.

7. Before term, have recourse to operation in pelves between 4.5 and 6.7 cm. in antero-posterior diameter, the labor being artificial and premature, as by compression the bi-parietal can be made 6.5 cm. Formerly in such cases abortion was the only recourse.

8. Embryotomy is not legitimate if fœtus be living and the woman at term, unless pelvis be below 6.7 cm.

9. Cæsarean section should not be practised in contracted pelves unless below 4 cm., except in place of embryotomy.

10. If consulted before term, and pelvis is under 8 cm., use premature labor and select that month of pregnancy which corresponds to the length of the bi-parietal diameter of the infant.

11. In oblique ovate pelves ischio-pubiotomy is preferable to symphysiotomy.

Le Page (*Archiv. Tocol. et Gynêcol.*, 1893, vol. xx., No. 5), at a meeting of the Société Obstetrique de France, April 7, 1893, presented notes of a case of symphysiotomy in a II-para for a pelvic tumor. Operation performed at the moment of dilatation with no especial difficulty, and a living child extracted. Labor went on normally after operation; forceps were used to deliver. Both mother and child made a good recovery. He formulates the following conclusions:

1. Symphysiotomy is an operation of urgency, practicable outside of maternities.

2. It is not merely of use in contracted pelves, but in normal ones if the fœtus be very large, or if pelvis is obstructed by tumors.

3. In the case reported, a premature labor at eight and a half months would have been insufficient. He thinks an accurate diagnosis should be made by touch before operating. The statistics of four other cases were presented for contracted pelves. All the mothers did well. Three of the children lived; one died during birth.

M. Budin reported a case where the above operation was done for a rhachitic pelvis. Promonto-subpubic diameter 9 cm., accompanied by general contraction of pelvis. Patient was a I-para and long in labor. Forceps had previously been tried. After operation the child was extracted, apparently dead, but was resuscitated and died eleven days after. Mother recovered.

Tellier (*ibid.*) reports a case, I-para, with pelvis of 10⅗ cm. promonto-subpubic diameter; pelvis *canaliculate*. When symphysis was cut there was

severe hemorrhage from branch of descending pubic artery (which, in this case, was as large as the radial), which caused much trouble. A living child was extracted with forceps; the symphysis separated 10 cm.; extensive tear of perineum and vagina anteriorly. The mother died from hemorrhage and shock. Autopsy showed nothing beyond the tears.

VARNIER discussed the application of the forceps at the superior strait in contracted pelves and its relation to symphysiotomy. Those of the school of Pinard maintained that without prior section of pubes this should not be done, as it involved the greatest dangers to the child and much to the mother. The section should be complete and include the subpubic ligament, and that the pelvis be dilated before final intervention.

BAR considered that version and moulding of the head should be tried in such cases. The value of induced premature labor was also pressed.

PUECH (*Nouveau Montpellier Medical*, 1893, p. 433), after a record of the history of symphysiotomy, states that it is owing chiefly to strict antisepsis that the operation has been once more brought forward. The only instruments necessary to the successful performance are two bistouries, some hæmostats, and it is well also to have a chain saw at hand to divide the symphysis in case of ossification. Besides these, the physician needs also the ordinary forceps and agents commonly used to resuscitate an asphyxiated child. He recommends that the incision be made about 8 cm. in length, and should be from above downward and from before backward, following the line of least resistance. It is of importance to divide the subpubic ligament. Some operators advise incomplete section of the bones or leaving the ligament uncut. This the author does not consent to. A cautious abduction of the thighs shows a separation. This should not be less than 4 cm. or more than 7 cm. The expulsion of the child should not be left to Nature, but accomplished promptly by means of forceps. Out of 61 cases of symphysiotomy, 51 were delivered by forceps, 10 being by the feet. A provisional antiseptic dressing should be put in the wound before the application of the forceps. Douches should afterward be given until the water returns clear.

In regard to sutures, he recommends that three or four deep ones of silver wire should be inserted close to the anterior face of the pubes, followed by a few superficial ones. There is no need for bone sutures. The thighs should be approximated, and, if necessary, a plaster splint can be applied. Stitches should be removed on eighth day; patient should remain in bed until the twentieth day.

In rhachitic pelves measuring over 6 cm. antero-posterior diameter, the enlargement obtained is more than that furnished in the normal pelves by the same degree of separation. This stretching may reach 6 cm. without lesion of sacro-iliac articulations. Considering only the antero posterior diameter of the bony pelvic ring, one sees that for a pubic separation from 5 to 6 cm. the diameter increases from 12 to 15 mm. in length.

With pubic widening of . . .	5 cm.	6 cm.	7 cm.
the gain is as follows:			
Pelvis . . . . 5 cm.	73 mm.	79 mm.	85 cm.
" . . . . 6 "	81 "	86 "	91 "
" . . . . 7 "	89 "	93 "	98 "
" . . . . 8 "	97 "	101 "	105 "
" . . . . 9 "	106 "	109 "	113 "
" . . . . 10 "	114 "	118 "	121 "

Mortality. Morisani, from 148 cases of symphysiotomy, gives a mortality of 27.72 per cent. maternal; 47.26 per cent. infantile.

The author, from 73 cases of operation, gives mortality of mothers, 4.1 per cent.; infantile, 24.6 per cent.

The operations were often done under the most unfavorable circumstances. We may also conclude that this operation is rarely followed by ultimate impairment of locomotion or micturition, and the lesions, small or serious, of the genitalia are not different from those that frequently follow difficult or prolonged forceps cases.

Symphysiotomy is best done at the time of complete dilatation. In view of the high mortality of the children where premature labor has been induced in women with contracted pelves, it is deemed best to allow such cases to go to full term and then operate. The chances of the child are thereby increased, provided the degree of narrowing is such as to make the cases suitable for symphysiotomy.

There is a new operation which ought to take its place with symphysiotomy and extend its field: this is ischio-pubiotomy in oblique ovate pelves with synostosis of one sacro-iliac joint. It consists essentially in section of the ascending ramus of the ischium and of the horizontal ramus of the pubis, with destruction of all opposing fibrous parts.

Puerperal Tetanus.

Heyse (*Deutsche med. Wochenschrift*, 1893, No. 14), after citing a number of cases suffering either primarily or secondarily from puerperal tetanus, states that it is interesting to note that the primary sources of infection in these cases were in nearly all either from those working in the ground or among horses. One can, however, only reckon true puerperal tetanus, those cases in which the bacillus has entered the uterus before or during labor. The claim that tetanus belongs to the group of infectious puerperal diseases has not always been admitted, as numerous attempts to inoculate the disease with endometritic material have failed. Cold, filthy surroundings, and wounds of the perineum or vagina have been insisted on as portals for the disease more probable than the necrotic uterine mucous membrane of the puerperium.

The question, whether tetanotoxin or tetanus bacilli capable of development and spores can be maintained in the lochia, is of great importance in regard to the prophylaxis of this disease. He then describes a case where a woman died with all symptoms of acute tetanus (puerperal), and on whom, after death, was found on the left side of the posterior commissure a small, deep, fresh granulating tear. Left from the introitus vaginæ was a small ulcer, with thin yellow coat over red granulations; edges smooth and round; no infiltration. No intra-uterine manipulation had been used in the case. Infiltration of the parametrium, or of Douglas's cul-de-sac, was not present. Urine contained albumin, hyaline, fatty, and granular casts.

Section showed heart-exhaustion; uterus as large as a child's head; serosa smooth and shining; muscle dull; no pus.

Cervix showed diphtheritic endometritis. At point of former attachment of placenta, fragments could be found. No thrombi in parametrium; no sign of infection passing beyond the uterine mucous membrane. In the brain

a subdural hæmatoma as large as the palm of the hand was found in the occipito-parietal region. Kidney negative.

Microscopic examination of the uterus showed on the inner wall of the endometrium small masses of staphylococci, but no tetanus bacilli were found. Inoculations of two mice with membrane taken from ulcers and uterus wall resulted in one animal dying of staphylococcus sepsis; the other lived. Five mice and one guinea-pig were injected with material taken during life from the cervix secretion on sterilized cotton. Great care was exercised in keeping this from contact with the ulcers and perineal rent. A mucous plug from the cervix was also withdrawn. All the animals thus inoculated had symptoms of tetanus, and all save one mouse died after seventy to ninety hours. A deep culture on sugar-agar was made in an incubator, and the development of anaërobic bacteria appeared in gas bubbles which came from the cotton. The presence of spore-bearing tetanus bacilli was shown directly from the cervical secretion, and guinea-pigs inoculated from this died; from them a tetanus culture was obtained.

If the lochia of a case of tetanus contains the characteristic bacilli and spores, the case may be regarded as sure.

A culture made from straw, dust, and floor boards, the first from the patient's bed and the remainder from the room in which she died, was injected into mice, all dying of tetanus. A grape-sugar agar culture showed the tetanus bacillus present with others, especially the staphylococcus albus and cereus.

VENAY records 106 cases of puerperal tetanus: 47 after abortion, 59 after delivery; the greater number being near the menopause. According to these statistics the disease may break out from two to fifteen days after birth; commonly from the seventh to eleventh. He considers its prevalence due to the fact that the bacillus lives in dirt, and gives as a cause of the number of cases in the West Indies the custom of the negroes of smearing dirt on the umbilical wound of the child.

Statistics show that it is not the greater operations that are followed by tetanus; tamponing and manual detachment of the placenta are those that are most dangerous.

Venay showed 107 cases: 51 were operative; 20 followed uterine curetting, 17 tamponing, 5 forceps extraction, 3 version and artificial premature labor, 1 each Cæsarean section and curettement. Puerperal tetanus shows a certain connection with puerperal septicæmia, in that it prevails most amid unfavorable surroundings. The reason for the small percentage after great operations is because patients needing these go to infirmaries. Septicæmia is not merely a complication of tetanus, but begets it. Observations seem to prove that the tetanus bacillus cannot thrive save in a prepared soil of some other disease, or it is a mixed infection. French observers maintain that a pure culture of the tetanus bacilli cannot be made if they are freed, by heating to 80°, from the toxin produced. The non-toxic cultures can only produce tetanus when other bacteria are introduced, generally pus-makers, which set up a necrotic inflammation, otherwise the spores fail and are taken up by leucocytes. The other pus-producers, after setting up a massing of leucocytes, form a sort of false membrane, which protects the tetanus bacillus.

A thorough clearing out of the uterus and careful disinfection under chloroform would seem the best treatment. Among medicines, Venay classes

narcotics first, then chloral, and chloroform. Absolute rest, hot baths, wet pack, and withdrawal of bright light and noise.

Eclampsia and its Treatment.

Martin (*Edinburgh Med. Journ.*, 1893, p. 1125) reports a case of eclampsia occurring in a mill-worker, twenty-one years of age. Family history good. Patient had complained of headache, especially in the morning. Labor was induced, and patient was delivered of a healthy child. The attacks occurred every twelve to sixteen minutes, and terminated fatally at the end of twenty-four hours. During the night preceding death the breathing was stertorous, and six hours before death Cheyne-Stokes respiration set in. No post-mortem could be obtained.

Porteous (*Edinburgh Med. Journ.*, 1893, p. 1162) advances the theory that there are five forms of eclampsia: (1) Hysteric, (2) epileptic, (3) uræmic, (4) apoplectic, (5) microbic. In the microbic there are none of the signs or symptoms of ordinary eclampsia. The kidneys are not at fault; temperature varies little, and the pulse neither quickens nor becomes slower for any length of time.

Achondroplasia (Chondrodystrophia Fœtalis, or so-called Fœtal Rickets).

Thompson (*Edinburgh Med. Journ.*, 1893, p. 1109), in an article on the above subject, states that many cases of the peculiar deformity often described in text-books as fœtal rickets, cannot be regarded as such. The disease is characterized by an unnatural shortness of the upper and lower limbs, and is separate and distinct from either rickets or cretinism. The cause of this affection is not well understood, but is supposed to be an absence, arrest, or perversion of the normal process of endochondral ossification of the most definite and universal character in every element of the skeleton in which the process normally takes place during intra-uterine life. It would seem that this disease was to some extent inherited. The writer regards as a peculiar feature of the disease that in the hand, when laid flat so that the palm is not hollowed, the fingers being spread out in such a way that their ends are separate from one another and not so close as in the normal hand, the index and middle fingers curve to the radial, the ring and little fingers to the ulnar side. In the article three cases are quoted, all having typical characteristics of the disease.

Investigation on the Anatomy of the Cervix.

Knüpffer (*St. Petersburg. medicin. Wochenschrift*, 1893, No. 13, p. 115), after a number of experiments on bats, has demonstrated that birth must ensue when the cervix has widened sufficiently for the descending part to make pressure on the nerve ganglia found at the point of the vaginal insertion; pressure on these ganglia producing contraction of the uterus. After a portion of the pregnancy has passed, the uterus rising beyond the upper border of the lateral ligaments, the enlargement of the cervical canal allows the ganglia to be forced nearer and nearer to the wall of the canal. As

gestation advances, the lower uterine segment is formed. The mesometric ganglia become more and more conspicuous, and the cervix not only expands upward but presses toward the mesometrium. The fundus continuing to arise, a mechanical stimulation of the upper ganglia takes place, causing the first light contractions. With the deeper descent of the fœtus, the cervix is stretched and the presenting part approaches the great ganglia, which are prevented by the mesometrium frow withdrawing, and the presenting part is allowed to press on the deep ganglia, which are more numerous and larger, and thus strong uterine contractions are set up.

Umbilical Septic Infection.

In a discussion before the Königliche Gesellschaft der Aerzte, in Budapest, Doctor (*Prager medicin. Wochenschrift*, 1893, No. 13, p. 157) stated that a great percentage of children suffer in early days from fever, etc., from infection of the navel stump. Eröss states that in the first year of life 43 per cent. of children had fever, and of these 22 per cent. were due to infection of the navel. From experiments, he concluded that the best results were obtained where the cord was cut quickly after birth and close to the body, leaving a stump only about 1 cm. long. The child should not be bathed for from three to six days after birth. He claims that by these means he reduced the number of cases 3.46 per cent. If the wound secretes longer than two or three weeks after birth, it is in a pathological condition. The quantity and quality of the secretion afford evidences as to the condition: if serous, it is due to a fungoid umbilicus; a purulent secretion usually arising from an infection either general or local.

It was also shown that not bathing the child might tend to produce an intertrigo about the umbilicus. Out of 1000 cases not bathed before the falling off of the cord, none had bad symptoms.

Bacteriological Examination of the Lochia.

Afanassiew (*Gaz. de Gyn.*, No. 167, p. 173) reports the results of bacteriological investigation of the lochia of 24 parturient women. Out of 68 examinations, he obtained cultures in nearly all the cases. The bacteria diminished in the vagina from without inward, and were fewest at the uterine cavity. They were living and culturable, notwithstanding daily washing of the canal with carbolized water of 2 per cent. strength.

The Effect of Compression of the Abdominal Aorta for the Relief of Uterine Hemorrhage.

Bishop, in a lecture delivered at the Ancoats Hospital, Manchester (*Lancet*, 1893, No. xvi.), recommends compression of the aorta in cases of uterine hemorrhage as the quickest and most convenient manner of checking it. Time in this condition is of importance, because the longer hemorrhage lasts, the longer it is likely to continue on account of the general relaxation of the uterine tissue. The uterine arteries, through the internal and common iliac, start from a common source, the aorta, and can be controlled with the greatest ease by pressure upon it. The general condition of relaxation, and par-

ticularly of the abdominal muscles, from the bleeding, greatly favors this method of relief. The hand sinks into the abdomen without opposition until the sacral promontory is reached, and immediately above and to the left the main artery is discovered by its pulsations. He gives an interesting account of the pathology of uterine hemorrhage, and cites two cases of post-partum hemorrhage in which compression of the aorta was successfully used.

Ectopic Pregnancy.

Smith (*New York Journ. of Gyn. and Obstetrics*, 1893, vol. iii., No. 5) reports an interesting case of a II-para (first child dead when born), to whom he was summoned on June 4, 1891. Patient had been seized with a terrible pain "while weeding a flower-bed." She located this attack in the right iliac region. During the following weeks she had repeated attacks, until August 22, when she died. At the autopsy a mass the size of an orange was found in the right iliac region, involving the Fallopian tube and broad ligament. At one point of this mass the wall had become so attenuated that rupture had taken place into the peritoneal cavity. During the early history of the case some doubt had existed in the minds of the author and his consultants as to the character of the trouble, so that an operation was not considered fustifiable.

Spontaneous Parturition.

Dass (*Indian Medical Gazette*, 1893, No. 5) reports the case of a Bengali woman, aged forty years, delivered in an erect posture of a mature child. She had done her ordinary duties up to the time of delivery. Loss of blood considerable. Placenta was said to have come away after an hour's time. In afternoon of same day she walked to a railroad station, a distance of two miles. That evening at 10 o'clock she started in a railroad train, riding a distance of ninety-seven miles. During this entire time she had to sit up in the car without sleep. She went through a normal puerperium. Child was said to have been killed by its head striking the floor during birth.

Cæsarean Section for Contracted Pelvis.

Bancroft (*ibid.*) describes a Hindu III-para who had had one abortion. On admission pelvic measurements were as follows: External—Crests, 9.25 inches; spines, 8 inches; conj. ext., 5.75 inches; centre of vertebral spine to right iliac spine, 7.25 inches, and to left iliac spine, 7 inches. Internal—Pelvis generally small, pelvic arch narrow, promontory of sacrum easily reached by finger, estimated oblique conj., 2.75 inches; marked diminution in left oblique diameter; pelvis diminished in size. Cæsarean section was done, and the patient was delivered of a healthy child. Placenta was attached to the right posterior wall. The cavity was dusted over well with iodoform, and five sutures of carbolized silk were inserted through muscular walls. Considerable bony thickening was found on the right side of the pelvis, diminishing the right oblique diameter. Patient made a good recovery.

PÆDIATRICS.

UNDER THE CHARGE OF

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ASSISTED BY

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ACQUIRED SYPHILIS OF CHILDHOOD.

IN a recent clinical lecture, reported in the *Medical Press and Circular*, 1893, PROFESSOR FOURNIER groups the sources of acquired syphilis in childhood under four heads: 1. Suckling; 2. Rearing; 3. Criminal Offences; 4. Medical Treatment.

1. *Suckling.* Many children are infected by their nurses; a fact too little recognized, although examples may be reckoned by thousands. In a first group of cases it is a syphilitic nurse that takes the child to suckle, and from a mucous tubercle upon her mouth or breast she infects her charge. In the second group, the nurse is at the same time offender and victim. In the course of her avocation she contracts syphilis, which she hands on to her charge. A healthy nurse may tend an infant which is healthy to all appearances, but she contracts the disease. In her turn she infects either her own offspring or others to whom she may act as a wet-nurse. At other times a healthy nurse takes charge of a healthy child, but she one day chances to give the breast to a strange child that is syphilitic, and she and her charge then become infected. This point the author insists upon, and he attributes to it an astonishing number of cases of syphilis. It is to be remembered, however, that the habit of employing a wet-nurse is very much more common in France than in our own country, where the practice is rapidly being superseded by the more convenient and safer expedient of bottle-feeding.

2. *Rearing.* The child may take syphilis from its family, from servants, from visitors and others.

a. It is often taken from the mother. If a woman contracts syphilis after delivery she may communicate it to her child in various ways, the most common being by the act of kissing.

b. The father is less often at fault, as he has little to do with the child.

c. The infant is often infected by its nurse, either by kissing or in some other way. In this connection it may be noted that many infants live much more in the society of the nurse than of the mother, especially among the better classes of society; hence the frequency of this method of contagion.

d. A child is often infected by other children. It is a common trick with children to put toys and other objects in the mouth.

e. The poison may be communicated by strangers, workmen, or visitors, and usually by the act of kissing.

f. One often sees cases of domestic contagion where from poverty the

utensils are few and are used in common. Thus cases have been contracted from infected feeding-bottles, sponges, and bedding. Vidal de Cassis has reported the case of a povery-stricken household where one cup was used by six children, four of whom contracted syphilis.

3. *Criminal offences* upon children, followed by syphilis, are rare; still, it is easy to find plenty of instances. At Lourcine one frequently meets with children of ten or twelve and even of six or four years of age who have contracted the disease in this way. This class of crime is not always due to criminal passion, but often to the superstitious belief that an affected person may thus get rid of the disease.

4. *Medical treatment.* As in the case of the adult, a child may be affected by the hands of a medical attendant, or by surgical instruments. Some years ago a veritable endemic of the disease was reported as the result of catheterism by a specialist. Circumcision is answerable for a certain number of cases of the disease, a fact first pointed out by Ricord. Bardinet, of Limoges, relates the case of a midwife who carried on her profession notwithstanding the fact that she had syphilitic lesions on one of her fingers. She infected no less than a hundred persons, directly or indirectly, in the small township of Brives. Lastly, there is vaccination syphilis, which is becoming of very rare occurrence from the general adoption of the animal lymph.

The Incubation of Varicella.

A recent observation of Gouget (*Revue mensuelle des Maladies de l'Enfance*, 1893, p. 120) reopens the discussion upon the length of the incubative period of varicella. According to German authorities this period varies from 13 to 17 days (13 to 14, Henoch; 14 to 15, Gerhardt; 13 to 16, Eichhorst; 13 to 17, Strümpell). Barthey and Lanné believe that it may even be prolonged to 19 days, while English writers fix a minimum of 10 days. In several more recent articles Talamon (*La Médecine Moderne*, August 6, 1891; *vide* The American Journal of the Medical Sciences, March, 1892, p. 358; *ibid.*, May 19, 1892, and January 28, 1893) fixes this period more exactly at 14 days. Steiner and d'Heilly have observed instances of much shorter duration (8 days in Steiner's cases, 3 days in a case of d'Heilly), but these observations were made in cases of the inoculated disease; and it is well known that the incubative stage of the eruptive fevers is shorter when they are transmitted by inoculation than by contagion. Talamon, indeed, observed the development of varicella in a child whose sister had been attacked three days before, but did not hesitate to reject the possibility of an incubation so short, believing that the contagion had been effected by the intermediation of germs from another source, perhaps that from which the sister herself had been infected.

Gouget, in turn, relates the following case: A female infant, aged two months and a half, entered the Hôpital Tenon December 6th with varicella of moderate intensity, which had begun the evening before. *Four* days later varicella declared itself in a boy of fourteen months, entered the 5th of December, and lying in the adjacent bed. The eruption remained discrete; there were no more than twenty vesicles well disseminated. *Four* days later, a little girl, four and a half months old, entered the 29th of November, and occupying the next

adjacent bed to the latter case, was taken in turn with confluent varicella. Hereupon the three patients were isolated and no new cases developed. It may be added that there was no varicella in the ward before the arrival of the first of these children, and that no focus of contagion appeared to exist in the neighborhood, for no case of the disease had been brought to the hospital for quite a long time, and none had presented itself subsequently.

Despite the marked variation from the classic type, it is impossible not to be struck by the exactly equal period of apparent incubation in the two latter children. The regular propagation of the affection from bed to bed is also significant. If the second case is disregarded, and the third only attributed to infection from the first case, the incubation would be only eight days, while on the other hand, if referred to the time before entrance to the hospital, the period would be at least sixteen days.

Looking upon the regularity, in a sense mathematical, which was presented in the extension of this little epidemic, and upon the absence of new cases after isolation had been secured, the author is inclined to think that the incubation was reduced to four days in these two cases, and that consequently, under certain circumstances more or less rare, this period may be much shorter than is ordinarily the case. As to these circumstances, it is quite difficult to determine anything definite.

PATHOLOGY AND BACTERIOLOGY.

UNDER THE CHARGE OF

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IMMUNITY.

NOTHING at present engaging the attention of pathologists seems destined to attract such universal attention or to be of such far-reaching benefit to practical medicine as the study of the problems connected with immunity and recovery from infectious disease. It would seem that at last, nearly a century after the first vaccination (May 14, 1796), the obscurity which has prevented any rational explanation of its protective action were to be penetrated, and that the near future might witness the application of similar preventive measures to many of the infectious diseases. Already suggestions for the treatment of some of these diseases, gathered from ascertained facts regarding immunity, have been followed, and in a number of cases with the most gratifying result. In view of these facts, it has seemed appropriate to present to the readers of THE JOURNAL, in a short resumé, some of the principal contributions upon which the prevailing theory of immunity is based.

This theory may be briefly stated as follows: It has long been known that much, perhaps the whole, of the pathogenic influence of bacteria is due to the action of poisonous substances produced by them in the process of their growth. These "toxins," as they have been called, are accountable for the fever, the prostration, and other general symptoms of the infectious diseases, as well as for the anatomical changes (lesions) in the immediate neighborhood of the growing germs. So long as they continue to be produced and to have unrestrained action the disease progresses. But hand-in-hand with the production of these poisonous substances there are produced (by the cells of the body, presumably) certain antagonistic substances which neutralize the toxic principles, and thus prevent their poisonous effect upon the body. These antagonistic principles have been called "antitoxins," and the extent of their production is supposed to measure the degree of immunity. The natural immunity of some species of animals to certain diseases would appear to depend upon the ability of those animals to quickly prepare the antitoxins necessary to neutralize the poisons of the diseases from which they are immune. Artificial immunity, induced by experiment, depends upon the introduction into the body of a sufficient quantity of the specific antitoxin to neutralize the specific toxin. Recovery from the self-limited infectious diseases depends upon the production by the body of the antitoxins necessary to neutralize the specific poisons of the disease.

In 1890, OGATA and JASUHARA published in the *Transactions* of the Medical Faculty of the Imperial University of Tokio, Japan (see *Centralbl. f. Bakt. u. Parasit.*, 1891, ix. p. 25) an account of some remarkable experiments performed by them with a view to determining the influence of the blood of animals naturally immune to anthrax upon the virulence of the anthrax bacillus. The frog, white rat, and dog all possess natural immunity to anthrax, and it was found that cultures of virulent anthrax bacilli when mixed with the blood of these animals, or when grown upon media containing their blood serum, lost their virulence, either not killing at all, or only several days after the death of control animals inoculated at the same time with anthrax cultures not so treated. They furthermore determined that the immunity natural to the frog could be induced in mice by the intra-peritoneal injection of a few drops of frog's or dog's serum. All the mice so treated withstood the anthrax infection when the protective injection was performed at any time between seventy-two hours before and five hours after the anthrax inoculation. They also demonstrated that of seven mice thus rendered immune, six survived an inoculation with virulent anthrax several weeks after the establishment of the immunity, showing the effect to be quite lasting. The blood of other animals not naturally immune to anthrax when similarly injected had no protective action.

In a subsequent paper (*Centralbl. f. Bakt. u. Parasit.*, 1891, ix. p. 597) OGATA relates the result of his efforts to obtain the substance of the blood conferring this immunity, and describes a method of preparing from the blood a substance soluble in water and glycerin, insoluble in alcohol and ether, but not decomposed by them, decomposed by the digestive juices, by warming to 45° C., and by acids, and capable of conferring immunity to anthrax. The glycerin solution of this substance was shown to preserve this power of con-

ferring immunity for a very considerable length of time. It was believed by Ogata to be of the nature of an enzyme, having the power to convert fibrin into peptone and starch into sugar.

Shortly before the appearance of the above-mentioned paper by Ogata, BEHRING and KITASATO (*Deutsche med. Woch.*, 1890, No. 49) published the results of some remarkable experiments demonstrating the power of the blood of animals, made artificially immune to diphtheria and tetanus, to confer that immunity to other animals and to act curatively even after the onset of symptoms of the respective diseases. Thus, a rabbit rendered artificially immune to tetanus was shown to withstand an inoculation of 10 c.c. of a virulent culture of the tetanus bacillus, one-twentieth of which dose was at the same time shown to be fatal to rabbits not thus rendered immune, and the blood of this immune rabbit was further shown to be capable of conferring immunity to mice, which are well known to be particularly susceptible to tetanus.

In 1887 BRIEGER had shown the presence in sterilized cultures of the tetanus bacillus of a substance capable of causing trismus, convulsions, and death when introduced into mice, and later (1888) this substance was obtained from the freshly amputated arm of a patient suffering from tetanus. As the bacilli do not become generally diffused throughout the body in tetanus, it became evident that the exhausting symptoms of the disease must be due to the poisonous effect of the substance above referred to. With these facts in mind and in the hope of throwing some light upon the *modus operandi* of the blood of their immune rabbit in conferring immunity to others, Behring and Kitasato exposed virulent cultures of the tetanus bacillus to the action of its blood serum for twenty-four hours, after which it was found that doses of the cultures so treated three hundred times greater than the fatal dose of the same culture before such treatment were innocuous. They were, therefore, led to conclude that the serum of an immune animal possesses a most potent neutralizing action upon the poisons of the tetanus bacillus.

Simultaneously with the publication of these experiments of Behring and Kitasato there appeared in the *Berliner klinische Wochenschrift*, 1890, No. 49, an article by BRIEGER and FRAENKEL on immunity from diphtheria, in which they described the induction of immunity by the inoculation of guinea-pigs with a three weeks' old bouillon culture of Loefler's bacillus which had been heated for one hour to a temperature of 60–70° C. They found that the immunity was not immediately produced, but was gradually developed, until, two weeks after such an inoculation, it became complete. Even after this time slight local diphtheritic inflammation was produced by inoculation of a virulent culture, but none of the animals died. The power of attenuated virus to thus gradually induce immunity to the virulent poison of a disease had previously been shown by Pasteur as regards anthrax and hydrophobia.

In an earlier paper (*Berl. klin. Woch.*, 1890, Nos. 11 and 12) Brieger and Fraenkel had described the specific poison of diphtheria and had found it to be an albuminous substance, a "toxalbumin," exceedingly powerful in its action, but deprived of its poisonous properties by heating to a temperature of from 55° to 60° C. Because the immunizing substance withstood a higher temperature than this without impairment of its activity, Fraenkel was led

to believe the toxic and the immunizing substances to be separate and distinct bodies. The exact nature of the protective substance was not determined.

Behring and Kitasato had not described the manner in which the immunity of their animals had been obtained in the first instance, but after the publication of the work of Brieger and Fraenkel, an article by BEHRING (*Deutsche med. Woch.*, 1890, No. 50) described at length five different methods by which this might be accomplished in the case of diphtheria:

1. The first of these was dependent upon attenuation of the virus, and was identical with the method employed by Brieger and Fraenkel.

2. In the second, rather old cultures of the diphtheria bacillus were treated with very weak solutions of trichloride of iodine, and after two inoculations with the resulting mixture the animals proved immune to virulent cultures.

3. The bacteria-free pleuritic exudate of guinea-pigs which had died as the result of inoculation with Loeffler's bacillus, when injected in small quantity into healthy guinea-pigs made them very sick for several days, but on recovery they were found to be immune.

4. In a few cases, animals which had been inoculated with virulent diphtheria culture recovered as the result of careful treatment (particularly with iodine trichloride); these animals were found to be immune, but it was discovered that injections of iodine trichloride alone had no immunizing action.

5. But treatment with small quantities of hydrogen peroxide on several successive days before inoculation produced a more or less perfect immunity. It was shown that the blood serum of animals immunized by any of these methods, though having no actual germicidal quality, was still in some way able to neutralize the poisonous effects of the products of Loeffler's bacillus, and it was further shown that treatment with this serum was quickly followed by amelioration of the symptoms, and that in this way recovery could be brought about after otherwise fatal doses of the virulent culture. The possibility of curing acute infectious diseases by treatment with the serum of immunized animals was thus suggested, and it was also suggested that the immunizing and curative principle of the blood serum acts as a chemical antidote, not as a germicide.

Working along the same lines as Behring and Kitasato, TIZZONI and CATTANI (various articles in *Riforma Medica* for 1890 and 1891, reviewed in *Centralbl. f. Path. Anat.*, 1891, ii., No. 16, 666), arrived at a similar result as far as the production of an artificial immunity was concerned, and they also demonstrated the power of the blood serum of an immunized animal to confer immunity to others. The smallness of the amount of serum necessary to the establishment of immunity suggested to them the probability that the neutralizing substance was of the nature of a ferment, in some manner disintegrating the toxins of tetanus. This theory, it will be remembered, had previously been advanced by Ogata. In a subsequent communication (*Centralb. f. Bakt. u. Parasit.*, 1891, ix., No. 21, 685) they recount experiments which bear out this supposition, and they conclude that the tetanus "antitoxin," as they now call it, is an albuminous body of the nature of an enzyme, but not identical with the fibrin ferment of the blood. Still further experiments (*Centralbl. f. Bakt. u. Parasit.*, 1891, x., Nos. 2 and 3), showed this to belong to the globulins.

While these researches regarding immunity to tetanus and diphtheria were

in progress in Berlin and Bologna similar experiments were being carried on in Munich with the virus of pneumonia, and EMMERICH and FOWITZKY (*Münch. med. Woch.*, 1891, No. 32, p. 554) succeeded in producing artificial immunity in rabbits by inoculation of very small quantities of virulent cultures of the pneumococcus, the dose each day being increased until the immunity was complete. They found the serum of such immune animals to be capable of curing rabbits and mice suffering from pneumo-septicæmia, if introduced soon after the onset of symptoms. No therapeutic experiments upon patients suffering from pneumonia were undertaken.

A similar immunity to pneumonia was obtained by the brothers G. and F. KLEMPERER (*Berl. klin. Woch.* 1891, Nos. 34 and 35) by the injection of sputum of convalescents from pneumonia, of pus from empyema complicating pneumonia, of cultures of the pneumococcus attenuated by heat, and of a glycerin extract of an agar culture. It was later shown that the blood serum of convalescents from pneumonia was also capable of conferring immunity to rabbits. The immunity produced by all these methods appeared to be identical. In general it was found to be developed in three or four days when the protective substance was injected into the veins, but only after two weeks when introduced subcutaneously. The duration of the immunity varied in different cases, but was in some as long as six months.

The protective substance was found to be incapable of curing animals suffering from pneumo-septicæmia, but, on the other hand, a distinctly beneficial effect was noted after injections of the serum of immune animals, the result of such injections being uniformly beneficial in twenty-four rabbits suffering from pronounced symptoms.

In searching for an explanation of these results, the Klemperers separated from cultures of the pneumococcus a toxalbumin, poisonous in large doses, but capable in small doses of conferring immunity in animals. This had, however, no germicidal action, nor healing quality, and they were led to believe the immunity produced in their experiments to be due to the development in the body, through the agency in some way of this toxalbumin, of an antagonistic substance capable of preventing the development of the disease. This substance they have called "anti-pneumotoxin." They believe the potency of the serum of immune animals to convey immunity and to act curatively on other animals affected with pneumo-septicæmia to depend upon its content of anti-pneumotoxin, not upon any germicidal action of the blood serum. So convinced were they of the correctness of this view that they ventured to test the therapeutic value of the serum of their immunized animals in cases of acute lobar pneumonia. Having demonstrated its harmlessness by personal injections, they employed it subcutaneously in six cases of pneumonia. In all there resulted a decided reduction of temperature and a slowing of the pulse and respiration. In two of the cases the temperature remained normal after the treatment; in the others it slowly rose again six hours or so after the injection. That they were not simply dealing with an antipyretic was shown by the entire absence of any noticeable effect on patients affected with typhoid fever.

At about this time the theory of antitoxins was strengthened by the report of experiments by EHRLICH (*Deutsche medicinische Wochenschrift*, 1891, Nos. 32 and 44) upon immunity from the poisonous effects of the two vege-

table alkaloids, ricin and abrin. The immunity was produced in each case by the addition of very small quantities of the poison to the food of mice, the dose being increased from day to day, until after six days of such treatment an immunity was induced which protected the mice from doses of ricin from 200 to 800 times stronger than the usual fatal dose, and from doses of abrin 400 times the strength of the ordinary fatal dose. In both cases the immunity protected from the local inflammatory reaction as well as from the general symptoms (diarrhœa, collapse). In seeking an explanation of this remarkable immunity, Ehrlich separated from the blood of his immune animals in each case a substance capable of completely neutralizing the action of the alkaloid. These he has designated "anti-ricin" and "anti-abrin." Injections of the blood of immune animals established an immunity varying in degree with the degree of immunity of the animal from which the blood was taken and according to the amount injected; in other words, according to the amount of anti-ricin or anti-abrin introduced; but the degree of immunity so produced was never comparable to that obtained by the method of feeding.

From his observations Ehrlich was led to believe that the antidote formed remained for some considerable time in the body, as the immunity produced was of some duration, though its exact duration was not determined.

Animals immune to ricin were found to be fully susceptible to abrin, and *vice versa*, showing the antidotes in each case to be specifically antagonistic to one particular poison only and not to produce any generally efficient immunity, and Ehrlich argues therefrom that the antidotes in the two cases must be separate and distinct bodies.

These experiments of Ehrlich are strongly suggestive of a purely chemical antagonism between the antitoxins formed in the blood of immune animals and the poisons of the infectious diseases from which they are protected, the analogy being complete in every essential particular between the immunity to the alkaloids ricin and abrin and that to the infectious diseases which have been the subject of similar study.

It is not the purpose of this review to present every item of proof of the theory whose development we have been tracing, but rather to show a sufficient basis for its use as a good working hypothesis. This was believed to have been shown at the time of which we have just been speaking (1891), and soon reports of interesting therapeutic applications of the principles of the theory began to appear, more particularly in the case of tetanus. As their result furnishes an important factor in support of our theory, they will form the subject of a subsequent notice.

The Blood in Purpura Hæmorrhagica.

Interesting light has recently been thrown upon the obscure pathology of purpura by observations made by Denys (*Centralbl. für allgemeine Pathologie und Pathologische Anatomie*, 1893, iv., No. 5, p. 174) in a fatal case of the disease. The patient, a woman, suffered for several days from gastro-intestinal disorder of indefinite nature until three days prior to her death, when she began to bleed profusely from the vagina, without apparent cause. She was not seen by Denys until six hours before her death, when she was found to

be excessively anæmic and to be covered with small hæmorrhagic spots of a dark-red color. There was only very slight fever (38.2° C.), no pain, and, notwithstanding great prostration, the mind was clear. Examination of blood taken from the finger-tip, with all the precautions necessary in such observations, showed marked diminution in the number of red corpuscles, and increase in the leucocytes. Peculiar small bodies, spherical in shape, and somewhat resembling the nuclei of white corpuscles, were present in considerable numbers. They showed no tendency to adhere to one another or to surrounding objects, and were believed to be fragments of disintegrating leucocytes. No blood plaques were seen, though carefully searched for, and Denys was led to believe them to have been entirely absent in this case. Cultures made at the autopsy (forty-eight hours after death) from the tissues and from the hæmorrhagic spots, and subsequent microscopic examination disclosed nothing of importance relative to a possible mycotic origin of the disease, though long slender bacilli were found in places alone in the tissues of the intestine, but not elsewhere.

[In so far as the absence of blood plaques is concerned, this case is in interesting accord with three others previously studied by Denys, in which diminution in the number of blood plaques was the most notable blood change. Should this observation receive corroboration the multiple hemorrhages in purpura would readily be explained, as the blood plaques are now generally believed to play an important rôle in coagulation. Slight lesions in the blood-vessels have heretofore been observed as constantly present in purpura. So long as blood plaques are abundant in the blood considerable lesions in the vascular walls may be of but slight significance, thrombi quickly preventing the escape of any considerable quantity of blood. But in the absence of these important factors in thrombosis degenerative changes in the bloodvessels ordinarily insignificant may readily permit very considerable hemorrhage. Denys very properly attaches no importance to the bacilli met with in his observations. The autopsy was performed too long after death to afford reliable results, and the micro-organisms were of too limited distribution to be of any real significance.]

The Prevalence of Cancer and its Increase.

In a communication to the Manchester Medical Society (*Medical Chronicle*, February, 1893), W. Roger Williams draws attention to the steady increase in the prevalence of cancer throughout the civilized world. His statistics are gathered chiefly from the records of Great Britain, and show that in England and Wales in 1838, the year after the passage of the Registration Act, 2448 deaths were attributed to cancer, or 1 in 140 of the total mortality; in 1890 the deaths due to it numbered 19,433, being 1 in 28 of the total mortality. Thus the proportionate mortality from cancer now is five times greater than it was a half-century ago. Williams estimates from the extent of its mortality and the average duration of the disease, that there cannot be fewer than 60,000 persons now suffering from cancer in England and Wales. The returns for Scotland exhibit a similar state of things, the proportion of deaths from cancer to the total mortality having increased from 1 to 35 in 1884 to 1 to 27 in 1889.

"In most civilized countries where statistical records have been kept similar increases have been observed. In Norway the cancer deaths increased from 32 per 1000 of the total mortality in 1877 to 60 per 1000 in 1886–87. In the Netherlands the increase was from 4.9 per 10,000 living in 1867–79 to 6.5 in 1884–88, and in Prussia from 3.1 in 1881 to 3.8 in 1887. Brussels is credited with an increase from 3.9 in 1864–73 to 4.2 in 1874–78, and in New York the rise was from 4 in 1875 to 5.3 in 1885.

"In all the above instances the augmented cancer mortality has coincided with progressive population, increased national wealth, and marked improvement in the general well-being. It seems to me impossible to regard these coincidences otherwise than as the result of cause and effect.

"It accords with his view that in Ireland—where the converse conditions have prevailed, viz., decrease of population and widespread poverty—the cancer death-rate has been much lower than in either of the sister countries, and for many years it has shown no such marked increase as in the latter, but has often remained stationary or has even declined."

Interesting facts about the increasing cancer mortality of Great Britain are that it has affected males to a much greater extent than females, and that for both sexes the percentage of cancer deaths in persons above fifty-five years of age is greater than formerly, showing that the increased mortality is chiefly among persons of advanced age.

The Association of Typhoid Fever and Acute Miliary Tuberculosis.

The association of distinct species of infectious micro-organisms ("mixed infections") has excited considerable attention of late as explaining the puzzling departures from the ordinary clinical history of some of the infectious diseases. So far as we are aware, the simultaneous occurrence of typhoid fever and acute miliary tuberculosis had not been noted until the recent report of such a case by Kiéner and Villard (*Comptes-rendus hebd. des Séances de la Société de Biologie*, 1893, v., No. 1, p. 14). Unfortunately, the history of their case is not given, but the autopsy and cultures from the spleen, which were most thoroughly studied, showed unmistakably to the minds of the authors the presence of the typhoid bacillus in association with widely distributed lesions of acute tuberculosis. An interesting feature of the case is the association of typhoid and tubercular ulcers in the small intestine. These could be distinguished by the presence of induration and the occurrence of miliary tubercles on the peritoneal surface of the tubercular lesions, and by their entire absence in the typhoid.

On the Hereditary Transmission of Tuberculosis.

In an exhaustive article of 152 pages, Gärtner (*Zeitschrift für Hygiene und Infectionskrankheiten*, 1893, xiii. 101) reviews the present status of our knowledge upon the heredity of tuberculosis and adds experiments of his own demonstrating the direct transmission of the germs of the disease in animals from parent to fœtus. The comprehensive nature of the article precludes the giving in this place of more than the briefest statement of the conclusions reached.

Two factors demand attention in every consideration of the influence of heredity upon the transmission of an infectious disease: the influence of inherited predisposition, and the possibility of direct transmission of the specific germs from the parent to offspring. A thorough consideration of the subject from every point of view leads Gärtner to assert the existence of a certain varying degree of predisposition in different persons as regards tuberculosis, showing itself in the more easy acquisition of the disease in some cases than in others, and its more rapid progress. All debilitating influences, whether of general or local action, increase this predisposition, and the same is true as regards mechanical injury and changes in the chemical constitution of the cells and fluids of the body. The predisposition established by any of these means may be transmitted in a measure to succeeding generations.

Because of the uncertain result which has followed efforts to experimentally attenuate the tubercle bacillus, Gärtner discards the idea that tubercle bacilli of different degrees of virulence occur in nature and are accountable for different degrees of severity of the disease.

In his experiments Gärtner made use of mice, canaries, and rabbits. From the frequent direct transmission of tubercle bacilli from the mother to the fœtus (or egg) in the case of these animals, he concludes that a similar transmission of the disease in the case of man is less infrequent than has been supposed. This view is borne out by the high mortality from tuberculosis during the first year, higher than at any other period of life and decreasing during the first five years in geometrical ratio (16, 8, 4, 2, 1). Furthermore, the absence of symptoms of tuberculosis in a newborn child is not to be regarded as evidence that it may not have acquired the disease by direct transmission from the mother in consideration of the slow development of the disease and of the probability that infection has occurred during the latter half of gestation.

This direct transmission of the disease is believed by Gärtner to come solely from the mother, for he found it impossible in his experiments to obtain infected offspring when the mother was healthy, even though the semen of the father was teeming with tubercle bacilli. Under these circumstances the disease was frequently transmitted to the generative organs of the mother, but never to the fœtus resulting from the contact.

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